Archives of Dermatology and Syphilology

VOLUME 25 MAY, 1932 NUMBER 5

ACHROMIA PARASITARIA

ITS TRUE NATURE AND ETIOLOGY

V. PARDO-CASTELLO, M.D.

HAVANA, CUBA

In June, 1923, I reported before the Forty-Sixth Annual Meeting of the American Dermatological Association [1] the observations on thirty-six cases of a skin condition which I called, after Jeanselme's original name, achromia parasitaria. The disease has been observed since then with fair frequency in Cuba, and it has been the subject of much discussion at the meetings of the Cuban Dermatological Society where the parasitic nature of the ash-white spots was doubted, until I succeeded in demonstrating the presence of mycelial threads in the deep part of the corneous layer.

In the United States little attention has been given to this subject aside from the efforts of Prof. Howard Fox to cultivate fungi from the scales of similar lesions. The general attitude in America has been one of doubt about the real parasitic nature of this condition, and the common impression seems to be that it is a partial depigmentation due to a score of different cutaneous inflammations.

In Europe, particularly in France, Russia and Italy, several reports and discussions have been published in the last three or four years, and there seems to be no unanimity as to the etiology of the condition. Some think that achromia parasitaria is nothing more than the result of the action of the short wave rays of the sun, tanning a normal skin and leaving apparently depigmented spots in such places on the surface as happen to be protected by a patch of pityriasis versicolor. To others, achromia parasitaria is a true depigmentation produced by the destruction of the parasites by the short wave rays of the sun. Still to another group, the depigmentation would be the result of the presence of the fungus itself.

In my report of 1923, it was stated that my collaborator, Dr. Martinez Dominguez, had isolated from six cases a fungus which was classified as an aspergillus. Subsequently, the same aspergillus but also other different fungi were isolated from other patients.

Submitted for publication, Aug. 3, 1931.

1. Pardo-Castello, V., and Dominguez, M.: Achromia Parasitaria, Arch. Dermat. & Syph. **9**:82 (Jan.) 1924.

In 1927, Professor Kistiakowsky of Kiev made a study of this condition which he reported under the title of "Achroma cutis postparasitaria."[2] According to him:

> Under the influence of ultraviolet rays, the healthy skin first turns red, then becomes pigmented. Parts of the skin, covered by patches of pityriasis versicolor, neither become red nor change their yellowish-brownish tint. A slight desquamation is usually observed in the beginning; in a few days it increases, and the spot loses its brownish color and becomes lighter. In two or three weeks, there has been desquamation over almost the entire patch, and the scales remain only on the edge, forming a corolla of scales. Later, even these scales disappear; the area becomes smooth and resembles healthy, normal skin, which has not been exposed to sunburn.

As may be inferred from the foregoing quotation, Kistiakowsky believes that the achromatic condition is due to contrast between the sunburned normal skin and the normal skin which, protected by the growth of fungi of pityriasis versicolor in its surface, has not been affected by the sun. In other words, the mass of mycelium and spores growing on the corneous layer acts as a filter and prevents pigmentation.

Further, Kistiakowsky concluded:

> After a careful study of the works of Jeanselme and Pardo-Castello, I believe that in these cases also, achromia is caused, not by the biologic influence of the fungus, but by its presence and physical qualities.

In 1929, Gougerot, Joyeux, Burnier, Paul Blum, Jean Meyer, Saïdmen, Sabouraud and Milian[3] expressed a similar opinion, although they differed in the interpretation of the facts. According to these observers, "The ultraviolet rays of the sun and of the electric lights discolor the colored patches of pityriasis versicolor." And further, they said, "The achromia is a true achromia and not a pseudo-achromia due to contrast between the normal and the surrounding brown skin." They concluded: "In a word, achromia parasitaria in our country is an atypical form of pityriasis versicolor."

In 1930, Gougerot, Joyeux and Arnaudet[4] reported a case of achromia parasitaria in a North African Arab in whom they found Malassezzia furfur; they classified the case in the same category as those found in Europeans. In the discussion of this case, Jausion said that more important than the unity or plurality of the fungi causing these achromic lesions, are their pathogenic properties, and he recalls the observations on the luminosensibilization provoked by the myco-

---

2. Kistiakowsky, E. W.: Pityriasis Versicolor and Ultraviolet Rays: Achroma Cutis Postparasitaria, Arch. Dermat. & Syph. **15**:695 (June) 1927.

3. Gougerot; Joyeux and others: Achromies "parasitaires" ou mieux epidermomycosis achromiantes, Bull. Soc. franç. dermat. et syph. **36**:1028 (Nov.) 1929.

4. Gougerot; Joyeux and Arnaudet: Un cas d' achromie parasitaire nord africain, Bull. Soc. franç. de dermat. et syph. **37**:110 (Jan.) 1930.

porphyrins extracted from the fungi of corn such as penicillums and aspergillus. As a consequence of this photodynamism, pigmentation is observed. In these achromias one finds inversely leukoderma, which could be explained only by the reversal of the photocatalytic reaction.

In a second article on the same subject, Kistiakowsky [5] concluded:

1. Malassezzia furfur dies under the action of the ultraviolet rays of the sun: the spores disappear first and then the mycelium. 2. Exfoliation ceases due to the disappearance of the parasite which provokes it. 3. The epidermic scales, the mycelium and the spores filter the ultraviolet rays, protect the skin and produce the white plaques (pseudo-achromia by contrast). 4. As a consequence, physical properties, not biologic, are the cause of the presence of white patches. 5. There is no white pityriasis versicolor in nature. 6. The correct designation of the condition reported (not a disease) should be "pseudo-achromia postparasitaria." 7. There are found in tropical countries many cases of parasitic diseases with achromic aspect. It seems that the mechanism of origin of the achromias is of a physical and not of a biologic character. This problem still exacts serious studies.

In 1930, Artom [6] reported the case of a youth 18 years of age with achromia parasitaria of the chest, apparently due to a preexisting pityriasis versicolor. Artom's most important contribution is found in his experiences leading him to ascertain that the achromia observed is due to true depigmentation and not to contrast with the surrounding skin browned by the action of the sun. He covered part of the skin with an opaque disk protecting it thus from the action of the short wave rays, and still achromic patches were observed to develop. He believes that the fungus has an antiphotosensitizing action, or that perhaps depigmentation is due to inflammatory phenomena.

In 1931, Mantarro [7] reported six cases of an achromic condition from which Hemispora stellata was isolated. He expressed his doubts about the mode of action of the fungus; whether it is physicomechanical by screening off the short wave rays, or whether it is biologic through active ferments or oxidizing substances, is still to be demonstrated.

Castellani [8] described achromia parasitaria as synonymous with tinea flava and stated:

In certain cases the fungus of tinea flava has, apparently, a deep, permanent or almost permanent, disturbing action on the pigmentation processes of the skin, and the patches may remain yellowish and depigmented for a long time after the fungus has been destroyed.

---

5. Kistiakowsky, E. W.: L'achromie qui apparait sous l'action des rayons ultra-violet du soleil sur le pityriasis versicolor, est-elle parasitaire ou post-parasitaire? Ann. de dermat. et de syph. **1**:1264 (Dec.) 1930.

6. Artom, M.: Contributo allo studio della pityriasis, versicolor acromizzante, Gior. ital. di dermat. e sif. **71**:1945 (Dec.) 1930.

7. Mantarro, G.: Epidermomicosis acromizzante da hemispora stellata, Gior. ital. di dermat. e sif. **72**:131 (Feb.) 1931.

8. Castellani, A.: Fungi and Fungous Diseases, Arch. Dermat. & Syph. **17**: 215 (Feb.) 1928.

Further on, in making the differential diagnosis with pityriasis versicolor, he gives among other reasons the following:

> . . . and finally the fungus in certain cases has a permanent or semipermanent disturbing action on the pigmentation of the skin, patches remaining light yellow or whitish after the parasite has been destroyed.

COMMENT

Since the description of Jeanselme's cases of "achromie parasitaire a recrudescence estivale," this condition has been reported under different names. After due consideration and differentiation from other similar conditions, particularly from pityriasis versicolor, I reported my first thirty-six cases in 1923. In this report, I limited my remarks to the description of the cases and to stating the belief that the condition was different from all superficial epidermomycosis, and even different from tinea flava of Castellani, from a mycologic point of view. I also stated that the fungi isolated by my collaborator had not been definitely proved as the causative agent of the disease.

In recent years, further observations and studies and also the opinions expressed by Kistiakowsky, Gougerot, Artom, Mantarro and others have led me to believe that achromia parasitaria represents a group of epidermomycosis due to different fungi, affecting more or less similar clinical pictures, but varying according to the individual, the race and the geographic location.

This group of dermatomycosis comprehends those cases reported as achromie parasitaire a recrudescence estivale, tinea flava, tinea alba, achromia parasitaria and perhaps many cases indistinguishable from pityriasis versicolor.

As to the achromia observed in these cases, it is my opinion that the action of the rays of short wave of the sun or of the electric lights play little or no rôle in its production, and that most likely it is due to biologic or perhaps mechanical action of the fungi themselves on the pigmentary mechanism of the skin.

This conception is based on clinical and pathologic observations which, I believe, are definite. The condition is often observed in Negroes with very black skins, on which the ultraviolet rays of the sun have little or no effect; furthermore, it is often found in the covered parts where the sun rays cannot reach, such as the chest, abdomen and back, although it is most frequently observed on the face. The achromia or depigmentation may in some cases last many months or years, and in at least one of my cases it has remained unchanged for the past eight years. This shows that there is permanent disturbance of pigmentation which can hardly be attributed to the action of the sun or to the contrast between a normal skin and a sun tanned skin. This permanent dyschromia retains the same ash-white color from the beginning and can be easily differentiated from vitiligo. Therapeutically, in many

cases the skin returns to normal when early treatment with strong antiparasitic remedies is used.

Pathologically, sections of the affected skin show the absence or diminution of pigment in the basal layer of the epidermis and the presence of scattered lumps of pigment in the papillary layer of the dermis and even deeper in the cutis. In some places numerous chromatophores loaded with pigment may be seen. This, in my opinion, points very strongly to a disturbance of pigmentation occasioned directly on the affected skin by the action of the fungus.

On the other hand, it has been observed that numerous inflammatory dermatosis, such as eczema, miliaria tropica, dermatitis seborrheica, impetigo and other streptococci infections, may produce as a sequela discolored patches, particularly on the face and legs, which are probably due to a disturbance of pigmentation as a result of epidermic inflammation.

Achromia parasitaria is in all probability not a definite clinical entity answering to one etiologic agent, but an epiphenomenon in the evolution of a group of epidermomycoses in which the etiologic fungi disturb the normal process of pigmentation of the skin.

"LA CACOMONADE"

THE MORBUS GALLICUS, TWO CENTURIES AGO

HON. WILLIAM RENWICK RIDDELL, LLD., F.R.H.S. (Lond.)
TORONTO, CANADA

Simon Nicolas Henri Linguet was one of the most extraordinary men of a very extraordinary period. Born in 1736 at Rheims, educated in Paris, well skilled in mathematics and a fine linguist, he became a soldier, a lawyer and a satirist. His life being in danger, he fled to England, but not receiving the attention he expected, he went to Brussels and then back to France. In the troublous times of the last two decades of the eighteenth century, driven by the enmity provoked by his satire, he resided alternately in France, England, the Netherlands and Austria; finally in the Terror he was condemned to death and went bravely to the guillotine, June 27, 1794. His writings are very numerous, chiefly legal, historical and philosophical, and practically all more or less satirical, the satire not being very bitter as a rule.

One of his lesser works not mentioned in the biographies has the title:

LA
CACOMONADE
ou
Histoire
Politique et Philosophique
DU MAL DE NAPLES
Par Simon Nicolas Henri Linguet
Ouvrage traduit de l'Allemand du docteur PANGLOSS, par le docteur lui-même, depuis son retour de Constantinople
À COLOGNE, 1766
Et À Paris
CHEZ LES MARCHANDS DE NOUVEAUTÉS
1797 [1]

Submitted for publication, June 17, 1931.

1. "The Cacomonade or Political and Philosophical History of the Mal de Naples, by Simon Nicolas Henri Linguet. A work brought from Germany by Dr. Pangloss, by the Doctor himself since his return from Constantinople. Cologne, 1766, and Paris, at the Novelty Dealers, 1797." Of course, the Lues received the name Mal de Naples, Naples disease, from its appearance at the siege of Naples by the French under Charles VIII beginning in 1494. The name of Syphilis was given it by Fracastorius publishing his Syphilidis sive de morbo Gallico at Verona, 1530 (Riddell: Hieronymus Fracastorius, Toronto, 1928, pp. 8 and 16). Jacques de Bethencourt first gave the name venereal disease (morbus venereus) in his New Penitential Lent, Paris, 1527.

The volume is a thirty-two-mo of 103 pages, well printed on good paper, and is well bound in contemporary half-calf. It is somewhat rare, but has some vogue from its humorous, semi-serious, "half in fun and whole in earnest" account of the Mal de Naples, Morbus Gallicus. It pretends to be the work of Doctor Pangloss,[2] "Almoner to the Baron de Thunderthentronck and teacher of Candide." The Doctor "was whipped along with his pupil and hanged by order of the Inquisition," the preface tells us—but not before he with his pupil went to China and found the Baron. On the Doctor's death, the manuscript of "La Cacomonade" was found among his papers: it is elaborately explained that the word is derived from the Greek adjective "kakos," meaning evil, and Leibnitz' "Monads," and it is used "in the sense of that incomparable man."

I do not intend to give all the contents of this amusing book, but to extract only so much as has interest for the student of syphilology historically.

It starts off with the statement that two famous twin sisters, les Véroles (the Poxes), divided the Empire of the world between them, in the time of Noah, the younger and smaller, La Petite Vérole (Small Pox) taking Africa, Asia and Europe and occupying herself in marring the beauty of the face, and the other, La Grande Vérole (Great Pox) contenting herself with America with its reptiles. She, however, was not content with the beauty of the face; "she attacked directly that which rendered this beauty useful or precious." For five thousand years they lived apart, and it was only in the fifteenth century that they wished to visit each other—by the Spanish fleet—and since then they seem determined never to part. They have agreed to work in common, dominating without jealousy all parts of the world.

The Genoese Christopher Columbus brought us the precious germ in 1493, along with the gold of San Domingo, since which time they have flourished together, and, well we know it, the younger making the greater progress.

The object of his book is "to purify the worship of Venus, to drive out the foul air which pollutes her temples and to cleanse her altars"; for that purpose he is to examine carefully the means of destroying this enemy, and this research demands an account of its nature and treatment.

At the present day, the former is the more interesting, and I give it practically in full.

---

2. Dr. Pangloss (from the Greek "pas [pasa, pan]" meaning all and "glosse," meaning tongue), one of Voltaire's best known characters. He appears in "Candide" as the incurably optimistic philosopher with whom the favorite maxim was ever: "Everything is for the best in this best of all possible worlds." He was the tutor of Candide. Candide lived in Westphalia in the Chateau of Baron Thunderthentronck.

Serious reflections have taught that the Cacomonade is a poison (a note says a "Virus"), phlogistic, corrosive, coagulant and fixed—phlogistic as it causes inflammations, corrosive as it attacks the skin and produces solutions of continuity, coagulant as it arrests the course of the Humors [3] which nature designs to flow freely, and fixed, because it is difficult to displace. "There you have the whole theory of Cacomonade, developed by one of its best historians: It is obviously clear, concise, intelligible."

There follows what to me is the most interesting passage: "Charlatans have sometimes intermeddled, to give some other theory. For example, a celebrated one appeared at Paris in 1727. He pretended that all diseases of humanity, including that with which we are now concerned, are produced by little animals (de petits animaux) which are introduced into the blood. According to this theory what is called a remedy is something composed of other small animals, irreconcilable enemies of the former; they vigorously set themselves to drive them out.

"Accordingly, the body of a sick man is a battlefield where prodigies of valor are displayed. Fever leads there her legions, La Cacomonade her coagulating infantry. Soon is seen arriving the Faculty armed with quinquina and quicksilver; it marshals in order the different corps of that redoubtable militia. The battle long continues to rage until the animalcules of quinquina achieve a victory over those of the fever or the corrosive mites are driven out by the metallic insects, unless, indeed —as most frequently happens—the field of battle itself, overcome by such combats, sinks into the earth, engulfing with it conquerors and conquered.

"If that view is not true, it is at least delightful, but the gravity of the leading doctors has proscribed it. Annoyed at seeing themselves reduced by it to be no more than colonels of regiments of rhubarb and senna, they have laid violent hands on all these little armies given them to lead. They would sooner be chiefs of blind corpuscles [4] than command many living legions. They have determined to leave to chance harmony in the Humors,[3] using wholly material instruments rather to bring it there in good order escorted by troops, active and well disciplined. The reproach has been cast on the Faculty: 'Is this not to prefer inaction to activity, death to life'?

---

3. The theory accepted with practical universality in the Middle Ages was that there were four humors in the body: (1) Blood, (2) Bile, (3) Phlegm and (4) Melanchole or Black Bile. On the proper mixture of these and their regular flow depended the health of the body: an excess of one or more was injurious as was any interruption of them. Our "good humor," "bad humor," "temperament," "distemper," "sanguine," "phlegmatic," "bilious," "melancholy," etc., are relics of the terminology of this theory, the connotation now being, of course, quite different.

4. What is meant is that the current theory made the medicines without life, operating by mechanical or chemical means and not living creatures.

"That system cannot be too much regretted. It would give rise to the most amusing hypotheses; metaphysics, physics, philosophy, medicine furnish more absurd ones but none more amusing. But we must reconcile ourselves to its loss; with a crowd of great men, we must hold that Cacomonade is a poison, corrosive, coagulant, phlogistic and fixed."

Then as to the origin of the disease, no doubt the Supreme Being in framing Adam for procreation "gave him organs as healthy and as perfect as his companion could wish." Three causes are generally considered to account for the degeneration: the air, food and excess.

As to the air, that of the country regarded as its birthplace is no more unwholesome than that of countries into which it entered only with the aid of man; its productions, far from being dangerous, furnish us with a remedy against many diseases, while libertinage can hardly appear without luxury and opulence, and these scourges were certainly unknown in that country which we had to seek for the plague which follows and punishes them in our own.

Nevertheless, these are the only things which could have influence in its birth, and each has strong advocates. Those are certainly in error who contend that the air alone of San Domingo is sufficient to produce this virus. For two hundred years and more, experience has proved that it is disseminated in precisely the way—and the only way—that it is in France. It grows there as it grows here in the midst of pleasure. Had the air anything of a contagious quality, it would have had its effect, since the conquest, on Europeans and Natives—and that does not happen.

Others contend that the disease comes from anthropophagy, as human flesh is itself a poison; but that is a rarer commodity than is generally supposed; moreover, the manner of life of those eaten by cannibals makes them very robust and healthy; consequently, it is absurd to suppose that their flesh in entering the stomach of others can acquire the faculty of poisoning them. "That would be a permissible revenge, but one does not take revenge when put on the spit."

An able physician, in a large book that he wrote, gave a third theory. He says that excess in hot countries and the small choice of companions available have caused the disease, and he adduces the following very curious particulars: "According to Tavernier,[5] the women of the Kingdom of Melinde [6] are so dangerous once a month that if a European

5. Jean Baptiste Tavernier (1605-1689), born in Paris, was a French traveler to Turkey, Persia, central Asia and the East Indies; his Travels were published in 1676 to 1679.

6. Melinde, or Melinda, is a town in British East Africa; it was successively an Arabian, Portuguese and Zanzibar trading-post. It is about 200 miles south of the equator. Nothing is known at the present time of the extraordinary influence of its women noted by Tavernier, and one is at liberty to be skeptical about it.

is so unfortunate as to be in a place where one has urinated at such a time, he is attacked with fever, headache and sometimes the plague." The author adds: "I must say in reading this passage that I ardently hoped that no woman of the Melinde would stop under my window."

Fortunately, Dr. A. says, this would not apply to our climate; but he thinks that there is a close relation between the origin of Cacomonade and the pestilential influence of the swarthy beauties of Zanzibar, and insists that the one is the cause of the other.

The inquiry then is made as to whether the disease was known to the ancients. The answer is in the negative. Homer could not have failed to depict Venus imploring the aid of Mercury; Hippocrates and Galen could not have passed the disease over; Tiberius, Caligula, Nero, monsters of lubricity, never had to use mercury; no poet, Latin or Greek, celebrates its virtues, and the greatest libertines had not to pay for excess in this way.

Had Job any personal experience with it? The learned priest, Dom Calmet, says: "Yes, he took it from his wife and she from the Devil." But, surely, it is enough for such a holy man to have such a bad wife, and why suppose that he had anything from her but insults? Of course when he sat among the ashes (the author makes it "fumier," dunghill) his skin was covered with ulcers "from the sole of his foot unto his crown," his skin was dry (so that he had to have a potsherd to scrape it with) and the Lord had curdled him like cheese; and these three are the principal symptoms of the Lues according to Dr. A. True it is, too, that after a long silence, Eliphaz, one of his friends, indirectly charged him with giving himself up to iniquity and reaping what he had sown—that he had loved the houses of dust and had been attacked by something not unlike the scurvy (teigne).[7] All that, however, proves that the Devil had four thousand years later to seek in America a grain of Cacomonade to inoculate a poor Chaldean. The probability, such as it is, "is not great enough to make us believe that Job ever had need of the fluid of the barometer."

Is lepra the same thing as Cacomonade? Historians of the Crusades of the twelfth and thirteenth centuries tell of lepra following these "edifying but cruel expeditions." But lepra affected the skin only by changing its color not by cicatrizing it, leaving only a strong inclination to scratch. It had previously been unknown to the Greeks, the Romans, the Gauls and the Germans; neither Asiatics, Persians nor Syrians knew of it. The Jews were accustomed to go trading to different parts of the earth, scratching all the time, but they left behind only their merchandise. They had perhaps white itchy patches and scratched themselves.

7. Job 2:3, ashes; 2:7, boils; 2:8, potsherd; 10:10, curdled; 4:8, reaping fruit of iniquity.

sweat profusely and bathed seldom, but one can hardly confuse the white patches, the itching, etc., with Cacomonade.

Moreover, lepra did not attack the genitals. The only resemblance that I can see between them is that each was brought into Europe after an expedition as unjust as it was sanguinary: "The Crusades and the rapine of the Island of Hispaniola are the two direct plagues with which humanity has been afflicted since Original Sin."

An inquiry is then made into the Regulations of Jeanne I, Queen of the Two Sicilies and Countess of Provence in founding, in 1374, a Convent for Women of the Town, which we may pass over as curious rather than important.

Of the introduction of Cacomonade into Europe, especially France, the author says: "Three centuries ago, a Genoese procured for us the pleasure of knowing America . . . and to pay too dear for it. . . . It is from that happy moment that our women have had perruques [8] and our sailors have had scurvy. . . . The first vessel that landed in Spain loaded with the production of the New World excited universal enthusiasm . . . there were seen displayed incarnate plumes red with the blood of Indians, earrings with the ends of the ears attached, rings with the fingers of their former owners, nose rings with the noses they long adorned."

The Argonauts of the sixteenth century took more pride in courage than in patience: "to take more quickly the jewels of the Caribs, they took at the same time the jewels and the carriers;" everything that could be turned into gold remained in their hands, but while the splendid cargo filled all with joy, no one noticed Cacomonade hidden behind the precious bales. The virtuous Queen Isabella with her husband, the generous Frederick the Catholic, had sworn to his father, the King of Naples, to defend him, and so they embarked troops at Barcelona to assist him—but with a new feature: Cacomonade was one of the principal articles; it went at the same time as the army; at first it made slow progress in Italy, but fortunately for it, Charles VIII took it into his head to visit Pope Alexander VI at Rome. Every one knows how brilliant and how futile this expedition was.[9] Our French chevaliers displayed a heroism most admirable, but most useless. They speedily took Milan, Florence, Rome, Naples and the Lues, but of all their conquests this last, by which they would most gladly have been defeated, is all that was left to them.

---

8. It will be seen later in the text that the origin of perruques (wigs) is traced to the baldness of Francis I of France, caused by syphilis.

9. The invasion of Italy by Charles VIII of France began in 1494; he conquered Naples, but retired precipitately in the face of the league of the Pope and the Emperor. He died in 1498 when he was preparing for another invasion (Riddell: Hieronymus Fracastorius, p. 16).

On their return, they transplanted it in their land, and it was almost the only fruit to our ancestors of so glorious a campaign.

As to the voyages of Cacomonade: On following to France so many valiant warriors, from time to time it escaped to form colonies elsewhere. It descended the Garonne to cast anchor in the Thames: it passed the Pyrenees across Spain to Portugal, and from Lisbon it went to Goa. It left Cadiz for Mauritania with some Jews or Mohammedans. Frederick the Catholic did not wish these in his Dominions. They penetrated the Torrid Zone in the midst of African sands; they entered Melinde, from the sources of Senegal to Cafraria, from Monomotapa to the embouchure of the Nile. It went from Marseilles into Syria and Egypt; it visited the seaports of the Levant; it went by way of the purchased Circassians, whom the law of Mohammed allowed to uncircumcised and true believer alike, found an entry to the home of the proudest Mohammedans of the sect of Omar. These charitably transmitted it to the heretical seed of Ali, who took it to the inhabitants of Mogul, adorers of Brahma and Vishnu, who employed junks to take it to Macao and Nagasaki, to the theologians of Fee and of Kaka. They touched in passing at Malabar, refreshed themselves at the Philippines and Molukka; there it is said there are those who intoxicate themselves with juice of the grape or apple or of barley sharpened by fermentation; others poison themselves with the same juice distilled by fire . . . others put a brown and unwholesome powder in their nose . . . all these and more are hers.

Women are seen who spread calcined lead on their face; others who color their cheeks and arms with indigo; others who expose their bosom, others who cover only their posterior; others who perfume and frizzle themselves to attract their lovers; others who give them the plague by remaining near them at a certain time—and all these are hers.

Nor should we forget that in her travels La Cacomonade took the livery and the name of the nation whence she came: She was "Neapolitan" in France, "French" in Naples and Madrid, "Castilian" at Lisbon, "Portuguese" at Nagasaki, "Turkish" at Ispahan and "French" again at Constantinople.

Then we have a chapter on the origin of perruques. Francis I took La Cacomonade beside him on the throne. "It cost him only fifty crowns, his uvula and his hair, but he had to speak low and cover his head." And so wigs were invented.

The empire of the perruque is, indeed, now diminished, but that of the mother is not.

As to the means of combating it, on its first appearance doctors were in despair. They treated familiar diseases with confidence, but here was a new face unknown to Hippocrates. True it made itself known by most alarming signs: One left his nose in his handkerchief; he spat out his

tongue and the glands that kept it fresh; throwing a stone, he was surprised to see his arm going with it; he found himself, in less than no time, reduced to the condition of the guardians of the Seraglio, in whom the Turks left nothing to excite even the breath of suspicion. The human race seemed doomed to destruction by this new form of attack.

In this emergency, the Faculty lost its head: "It was not a case in which the Doctor could with hot water and eloquence take credit for the operation of nature." Physicians stood aghast and helpless.

But men without a degree, charlatans more daring and more greedy than the doctors, undertook the combat; and if they could not assure victory, they could at least sell hope. Experiments were made, vegetable infusions and chemical compounds were tried, China and America were laid under tribute and Hippocrates was quoted, but no light appeared.

At length, as so often occurs, chance came to the aid of science: A white fluid was known, like silver, but heavier, and known to have a faculty of attaching itself to other metals—for it was counted among the metals, one scarcely knew why. No one could imagine that by grinding it up with lard and applying it to the skin, or by giving it to swallow mixed with other ingredients, it would put the intruder to flight. It is said, indeed, that some of the Arabians had made use of it for lice and herpes, to alleviate itching and in other skin diseases, but its use was unknown in Europe, and though Avicenna and Serapion [10] spoke of it, no one could imagine that a specific for lice would be useful in the Lues.

Fought against by the Faculty most rigorously, the use of mercury spread and is now universal; just as is the use of (tartar) emetic, of quinquina, of ipecacuanha, and other drugs decried by the predecessors of those who now constantly employ them.

A chapter follows containing a dialogue between a Chinese Mandarin who had caught the infection from "a very handsome woman with a very small foot," who had come in on the last ship, and Baron de Thunderthentronck whom he asked to cure him. The Baron suggests Inunction with Neapolitan unguent made of mercury and lard. It afforded some hope of cure, but had its inconveniences. He tells the Mandarin: "Your head will swell enormously; your teeth will get loose and perhaps fall out; your gums and throat will ulcerate; you will be

10. Avicenna (Ibn Sina), born in Bokhara in 980, died in Persia in 1037; he was the most celebrated of the so-called Arabian physicians, and was noted for his Commentaries on Aristotle and his translation of Galen; his works on medicine had great vogue until well into the sixteenth century (Baas, J. H.: Outlines of History of Medicine and the Medical Profession, translated by H. E. Handerson, New York, 1889, p. 229). There were two Serapions. One, called Serapion the Elder (802-849), of Damascus, was one of the first to deal with diseases of the head. His theory of hysteria is not quite forgotten. The other, Serapion the Younger, who died in 1070, was once known by his work on "Simple Remedies" (Baas: ibid., pp. 226 and 230).

salivated; you may lose an eye or an arm or a leg or the uvula, like the late king Francis I of glorious memory and many others of less note and no greater good fortune." Naturally, the Mandarin declines this treatment, and the Baron proposes to moderate it, proceeding by "Extinction," massaging gently and administering milk sometimes to alleviate the effects. The patient would spit less, swell less and stink less, but the greatest danger would be that he would not be cured. So that is not at all acceptable.

Then the Baron suggests Fumigation: "You are seated nude in a pine box with only the head protruding; below is a lighted chafing-dish with mercury on the coals. The fluid, volatilized by the fire and kept in by the box and the heavy cloak covering, gradually penetrates the pores. You will perspire freely and perhaps in the end you will find yourself cured. Some have been so fortunate."

Even that does not suit the Mandarin. But the Baron is not at the end of his resources. He says: "You might be treated with panaceas, with different kinds of aethiops mineral;[11] we might give you a weak solution of a salt of mercury, or tinctures of gold and silver. I have not all of these, but our apothecary can supply you with them."

The Mandarin, exasperated, exclaims: "For Heaven's sake, stop telling me what I may do and tell me what I should do!" "Here," says the Baron, "you see this little red box? In your place I should use that." The little red box was full of gray pills, Keyser's Dragées.[12] "Keyser," says the Baron, "is a German physician, my countryman, who has contrived a wholly new composition against this plague. . . . Use it under my directions and you will certainly be cured. . . . I am so sure of that that I shall not ask for my fee of a hundred pounds of tea until you are cured." And the treatment began at once.

The last two chapters deal with the means of suppressing the evil, now of little or no interest.

No one can read this little book without recognizing the wide range of knowledge, the acumen and the humor of the author.

Osgoode Hall.

---

11. "Aethiops mineral" is defined by an old writer thus: "A Medicine made by Imbodying equal parts of running Quicksilver and Flower of Brimstone and then Deflagrating or Burning off the Mixture in a Crucible."

12. A "Dragée" is a sort of sugarplum or sweetmeat in the center of which is a drug, and it is intended for the more ready taking of the medicine. Keyser's Dragées were a quack medicine having some vogue at the time for the cure of syphilis; they were composed of acetate of mercury, manna, starch, mucilage and gum tragacanth.

CHEMOTHERAPEUTIC STUDIES OF ACETARSONE (STOVARSOL)

GEORGE W. RAIZISS, PH.D.
Professor of Chemotherapy, Graduate School of Medicine, University of Pennsylvania
AND
M. SEVERAC, M.D.
PHILADELPHIA

In a recent article [1] dealing with 3-acetyl-amino-4-hydroxyphenyl-1-arsonic acid, generally known as acetarsone or stovarsol, we expressed the view that the problem of the toxicity of this compound requires reconsideration, since we found lower values for the toxicity of acetarsone than those heretofore obtained by other workers in this field.

Soon after the discovery of the antisyphilitic action of this preparation, conflicting reports regarding its toxicity appeared in the literature. When, in 1922, Levaditi, Navarro-Martin and Fournier [2] first recommended acetarsone (stovarsol) for use in the treatment for syphilis, they stated that the lethal dose of the drug, when given to the rabbit by mouth, is 0.6 Gm. per kilogram of body weight, but that a dose of from 0.3 to 0.4 Gm. is easily tolerated by the animals, some rabbits having tolerated well even 0.7 Gm. of stovarsol per kilogram. When, however, the toxicity of the preparation was tested by Collier and Evers, of the "Georg Speyer Haus," Frankfurt, Germany,[3] it was found that even a dose of 0.05 Gm. of stovarsol per kilogram was not always tolerated by rabbits: of five animals given orally 0.05 Gm. per kilogram, only two survived; of eight receiving 0.1 Gm., only one survived; and of eight given 0.2 Gm. per kilogram, only one survived.

As a result of the findings of Collier and Evers, a controversy arose regarding the toxicity of stovarsol, and several investigators took up the problem. It was found that Ehrlich and Hata were in possession of this compound before they synthesized arsphenamine, but they had

Submitted for publication, June 5, 1931.

From the University of Pennsylvania and the Dermatologic Research Laboratories.

1. Raiziss, G. W.; Severac, M., and Moetsch, J. C.: Toxicity of Acetarsone (Stovarsol), J. Chemotherapy **7**:1 (April) 1930.

2. Levaditi, C.; Navarro-Martin, A., and Fournier, L.: Recherches sur l'action curative et préventive de stovarsol administré par la voie digestive dans la syphilis, Ann. Inst. Pasteur **36**:729, 1922.

3. Collier, W. A., and Evers, E.: Untersuchungen über die Heil- und Schutz-Wirkung des Stovarsol, Dermat. Ztschr. **44**:1 (May) 1925.

apparently rejected it. Schlossberger,[4] therefore, tested the toxicity of Ehrlich's original preparation; the results were identical with those of Collier and Evers: oral doses of 0.1 Gm. per kilogram and above proved lethal.

Worms [5] performed a series of experiments both with the French stovarsol and with a German preparation identical with that of Ehrlich and Hata. He also found that the dose of 0.1 Gm. per kilogram was frequently toxic, although in some cases the dose of 0.33 Gm. was well tolerated.

Poole [6] who tested the original preparation of the French investigators, found that doses of 0.2 Gm. per kilogram and higher were toxic, and resulted in the death of the animals within twenty days.

Recently, Anderson and Leake,[7] experimenting with acetarsone of American production, found it toxic for rabbits when given per os in doses of from 0.125 to 0.175 Gm. per kilogram.

TABLE 1.—*Toxicity of Acetarsone (Stovarsol) as Determined by Various Investigators*

	Dose per Kilogram of Body Weight			
	Rabbits Intravenously		Rabbits per Os	
Author	Tolerated, Gm.	Lethal, Gm.	Tolerated, Gm.	Lethal, Gm.
Levaditi and Navarro-Martin.....	...	...	0.3-0.4	0.66
Collier and Evers.....	0.3	0.4	Less than 0.05	0.1
Ehrlich's preparation; Schlossberger	0.3	0.4	...	0.1
Poole.....	...	...	...	0.2
Anderson and Leake.....	...	...	...	0.125 to 0.175

As a result of these investigations, a considerably higher toxicity was attributed to this drug than was originally ascribed to it by Levaditi and Navarro-Martin. The aforementioned results are summarized in table 1.

Our own experiments, however, are at variance with such a view. In fact, by experimenting with acetarsone prepared by us, we have obtained values for its toxicity which are even more favorable than those of Levaditi and Navarro-Martin. This preparation was found to be well tolerated by rabbits when administered orally in a dose of 1 Gm. per kilogram,[8] the lethal dose being 1.5 Gm. In the same

4. Schlossberger, H., quoted by Collier and Evers (footnote 3).

5. Worms, W.: Weitere experimentelle Untersuchungen zur Stovarsolfrage, Deutsche med. Wchnschr. **51**:428 (March 13) 1925.

6. Poole, A. K.: A Note on the Prophylactic and Therapeutic Activity of the Sodium Salt of Stovarsol, Bull. Johns Hopkins Hosp. **38**:242 (March) 1926.

7. Anderson, H. H., and Leake, C. D.: Toxicity of Stovarsol, Proc. Soc. Exper. Biol. & Med. **27**:267 (Jan.) 1930.

8. These figures were obtained with exceptionally good samples. The average maximum tolerated dose is 0.8 Gm.

experiment, acetarsone obtained on the market proved lethal for rabbits in the dose of 0.5 Gm., while it was tolerated in the dose of 0.4 Gm. per kilogram.

We have also tested the toxicity of the sodium salt of our preparation intravenously administered. Rabbits tolerated a dose of 0.5 Gm., while a dose of 0.6 Gm. was fatal. It is interesting to note that Collier and Evers have found that the sodium salt of Ehrlich's stovarsol was lethal for rabbits, when 0.4 Gm. per kilogram was injected intravenously, while a dose of 0.3 Gm. was tolerated. Our results are summarized in table 2.

It is thus seen that the acetarsone used in our experiments could be given to rabbits by mouth in doses two and one-half times as high as those administered by Levaditi and Navarro-Martin, the lethal dose in our case being 1.5 Gm. and the maximum tolerated dose 1 Gm.

TABLE 2.—*Toxicity of Acetarsone (Stovarsol) Determined by Raiziss and Severac*

	Dose per Kilogram of Body Weight					
	Rats Intravenously		Rabbits Intravenously		Rabbits per Os	
Drug*	Tolerated, Gm.	Lethal, Gm.	Tolerated, Gm.	Lethal, Gm.	Tolerated, Gm.	Lethal, Gm.
Acetarsone (first test).....	0.3	0.4	...	...	1	1.5
Acetarsone (second test)...	0.25	0.3	0.1	0.12	1	1.5
Stovarsol.....	...	...	...	...	0.4	0.5
Sodium salt of acetarsone.	0.7	0.75	0.5	0.6	0.8	1

* The acetarsone was prepared at the Dermatological Research Laboratories; the stovarsol was acquired on the market.

per kilogram. The difference between our figures and those of other investigators is still greater.

It now becomes of interest to consider the possible causes of these variations in experimental results. Fourneau was of the opinion that he had obtained better results with 3-acetyl-amino-4-hydroxyphenyl-arsonic acid because of the greater chemical purity of the preparation which he used, as compared, for instance, with the sample used by Ehrlich. This view is substantiated by the fact that the toxicity of an intermediate substance, 3-amino-4-hydroxyphenyl-arsonic acid was found by Fourneau and Navarro-Martin [9] to be much less than the value given by Ehrlich and Hata. Unfortunately, Ehrlich and Hata did not publish any data regarding the toxicity of the stovarsol itself, so that a direct comparison cannot be made.

We are inclined to believe that the cause of the lower toxicity of our preparation as compared with that of other investigators is its

9. Fourneau, E.: Sur l'emploi de l'acide oxy-aminophenylarsinique, Ann. Inst. Pasteur **35**:571, 1921. Navarro-Martin, A.: Sur l'emploi de l'amino-phenolarsenate de soude (189) dans le traitement de trypanosomiasis, Ann Inst. Pasteur **36**:38, 1922.

greater chemical purity. We have modified the method of preparation of acetarsone in the final stages, as well as in the preparation of the intermediate substances, and apparently have obtained a product of still greater purity than the preparation of Fourneau.

While low toxicity is a factor of great importance, nevertheless the value of an arsenical compound must depend largely on its trypanocidal and spirocheticidal properties. It becomes of interest, therefore, to analyze the value of acetarsone in experimental trypanosomiasis and its prophylactic and curative properties in experimental syphilis in rabbits.

ACETARSONE IN EXPERIMENTAL TRYPANOSOMIASIS

Fourneau and his co-workers [10] found that stovarsol had no or little effect in experimental trypanosomiasis; this result was later corroborated by Collier and Evers.[3]

Levaditi and Navarro-Martin tested stovarsol on mice infected with Trypanosoma brucei. The drug had no effect when it was introduced intravenously, and the results were only slightly better when it was given by mouth. Collier and Evers tested stovarsol on rabbits infected with Trypanosoma brucei subcutaneously as well as on rabbits infected either with the same organism or intracutaneously with Trypanosoma equiperdum; the latter infection produced chancres in the rabbits. Stovarsol was given to the animals per os in doses ranging from 0.05 to 0.25 Gm. per kilogram of body weight at various intervals before and after inoculation, as well as simultaneously with it. In only a few cases of subcutaneous inoculation was a prophylactic or curative action apparent. In none of the animals infected intracutaneously was the appearance of a chancre prevented. Moreover, the doses used proved toxic, and a greater part of the animals died of drug intoxication.

In our experiments the determination of the trypanocidal activity of acetarsone was made by the Voegtlin method with certain modifications described in one of our previous articles.[11] Rats were infected with Trypanosoma equiperdum, and acetarsone was administered intravenously twenty-four hours later. The peripheral blood of the animals was then examined for the presence of trypanosomes every day for twenty-one days. For purposes of comparison, another group of rats was simultaneously infected with the same amounts of trypanosomes and treated with arsphenamine in doses of 0.002, 0.004 and 0.006 Gm. per kilogram of body weight. The results are given in table 3. An inspection of table 3 shows that the minimum therapeutic dose for

10. Fourneau, Navarro-Martin and Trefouel: Les dérivés de l'acide phenylarsinique dans le traitement de trypanosomiasis et de spirilloses expérimentales, Ann. Inst. Pasteur **37**:581 (June) 1923.

11. Raiziss and Severac: Standardization of the Trypanocidal Test and of the Trypanocidal Value of Arsphenamine, Arch. Dermat. & Syph. **18**:263 (Aug.) 1928.

acetarsone was found to be 0.12 Gm. per kilogram of body weight; since the maximum tolerated dose is 0.25 Gm., the chemotherapeutic index is 2.

$$\frac{\text{0.25 Gm. per kilogram maximum tolerated dose}}{\text{0.12 Gm. per kilogram minimum curative dose}} = 2$$

The corresponding figures for arsphenamine are 0.006 and 0.160 Gm., yielding a chemotherapeutic index of 27, about thirteen and one-half times as great as that of acetarsone. Our findings are therefore in complete agreement with the conclusion of other investigators that acetarsone is of little value in experimental trypanosomiasis.

THE PROPHYLACTIC ACTION OF ACETARSONE IN EXPERIMENTAL SYPHILIS IN RABBITS

The first studies of the prophylactic properties of stovarsol administered orally were those of Levaditi, Navarro-Martin and their associ-

TABLE 3.—*Acetarsone (Stovarsol) in Experimental Trypanosomiasis*

Drug	Dose per Kilogram of Body Weight, Gm.	Result of Blood Examination*																			
		Hours			Days																
		24	48	72	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Acetarsone	0.080	—	+1	+2	+4	D																
	0.100	—	—	—	—	—	—	+	+2	+4	D											
	0.120	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Arsphenamine 47825	0.002	+3	+4	+4	D																	
	0.004	few	+1	+3	+4	D																
	0.006	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

* In this and subsequent tables, — indicates the absence of trypanosomes; +, the presence of trypanosomes; +1, a few trypanosomes; +2, numerous trypanosomes; +4, very numerous trypanosomes, and D, death of the animal.

ates.[2] Twenty-five rabbits were infected with syphilis and then given by mouth one or two doses of from 0.1 to 0.7 Gm. of the drug per kilogram, two hours, six hours, one day or seven days after inoculation. In none of the animals thus treated did syphilitic lesions develop, while the controls, simultaneously inoculated, became syphilitic.

These experiments were repeated by Collier and Evers,[3] but the preparation that they used proved to be so toxic that doses of even 0.1 Gm. frequently killed the animals. However, of four animals given 0.1 Gm. two hours after inoculation, chancres developed in three that did not die of drug intoxication. Five animals were given 0.1 Gm. one day after inoculation; in the only animal that survived, a chancre developed forty-six days later. These authors also made experiments with repeated smaller doses. Thus, five rabbits were given the dose of 0.075 Gm. per kilogram twice, on the first and on the third or fourth day after infection, and each of eight rabbits received a dose of 0.025 Gm. three times: one hour, one day and two days after infection. Of

the first group, only one rabbit survived; a chancre rich in spirochetes developed 160 days after infection. Of the second group, two animals survived, both remaining apparently normal.

Worms [5] investigated the prophylactic properties of acetarsone on sixteen rabbits, using the stovarsol of the French investigators as well as the corresponding product of the German workers, known as spirozid. His results were similar to those of Collier and Evers. Only two of eight animals given 0.25 Gm. of stovarsol or spirozid per kilogram two hours after inoculation gave evidence of protection (the time of observation was from four to five months), while in two a syphilitic infection developed, and five died of drug intoxication. Smaller doses (0.033 and 0.017 Gm.) did not prove prophylactic even when given repeatedly, except in one case. These results are rendered still less favorable by the statement of Worms that the Nichols strain of Spirochaeta pallida used in his experiments is more susceptible to arsenicals than the Truffi strain used by Collier and Evers.

Poole [6] administered orally 0.5 Gm. per kilogram of the stovarsol of the French investigators to six animals, two hours after intratesticular inoculation with the Nichols strain. Four of these animals died of drug intoxication twenty-one, fifty-one, fifty-one and sixty-six days afterward. In none of them, however, could spirochetes or visible manifestations of syphilis be detected. Other normal animals inoculated with the lymph nodes and testicles of these rabbits did not show any manifestations of syphilis. The two rabbits that survived remained free from any signs of infection. When these animals were reinoculated on the seventy-eighth day, orchitis developed, and spirochetes were present in the lesions; according to some authorities, such a successful reinoculation is proof of the absence of infection in the animals at the time of reinoculation.

Fischl [12] gave to rabbits 0.5 Gm. of spirozid per kilogram four times within two days (a total of 2 Gm.), and infected them with the Truffi strain twelve hours after the last dose was administered. The animals remained normal during six months of observation.

Thus, while it was found by Levaditi that a dose of 0.1 Gm. per kilogram can prevent the development of a syphilitic infection in the rabbit, this was not the case in the experiments of Collier and Evers. In Worms' experiments, even 0.25 Gm. was only partially effective (in 25 per cent of cases), while Poole obtained a prophylactic effect by using a dose of 0.5 Gm., which was close to, or above, the toxic dose. The same was true in the experiments of Free, who gave to each animal four doses of 0.5 Gm. per kilogram. As a result, the value of acetarsone

12. Fischl, V.: Die Ergebnisse experimenteller Prüfung der Oxyacetamino-Phenylarsinsäure, Klin. Wchnschr. **8**:1414, 1929.

as a prophylactic in syphilis was questioned, particularly since toxic doses were required to effect prophylaxis.

The prophylactic properties of the acetarsone that we prepared was determined in the following manner: Ten rabbits were infected with the Nichols strain of Spirochaeta pallida, each animal being inoculated with 0.5 cc. of an emulsion prepared from a testicle of a syphilitic rabbit with numerous very active spirochetes. In three animals used as controls pronounced syphilitic lesions developed in from 21 to 35 days. The remaining seven rabbits were given acetarsone by mouth immediately after infection, the dosage being 0.05 Gm. per kilogram of body

TABLE 4.—*Prophylactic Effect of Acetarsone Administered per Os in Experimental Syphilis in Rabbits*

Number of Animal	Method of Administration	Dose per Kilogram of Body Weight, Gm.	Primary Lesions of Testes and Scrotum	Generalized Lesions	Time of Popliteal Node Transfer	Results of Popliteal Node Transfer
285	Per os	0.050	None	None	After 105 days	Normal for 42 days (died)
321	Per os	0.050	None	None	After 98 days	Normal for 112 days
322	Per os	0.050	None	None	Animal died after 35 days (diarrhea)	
439	Per os	0.050	None	None	After 105 days	Normal for 112 days
440	Per os	0.050	None	None	After 98 days	Normal for 112 days
457	Per os	0.050	None	None	After 119 days	Normal for 112 days
458	Per os	0.050	None	None	After 105 days	Normal for 105 days
2474	Per os	0.025	Large, hard nodes in both testes with numerous spirochetes	None		
2475	Per os	0.025	.....	None		
2476	Per os	0.025	.....	None		
2473	Per os	0.010	Large, hard nodes in both testes with numerous spirochetes			

weight. The animals were kept under observation for periods ranging from 98 to 119 days. In none of the rabbits that received acetarsone did syphilitic infection develop. The popliteal nodes of all rabbits, except of one that died were removed according to the method of Brown and Pearce, and emulsions prepared from them were injected into the testicles of normal rabbits. This was done to eliminate the possibility of latent infection in the rabbits infected with syphilis and treated prophylactically with acetarsone administered per os.

More recently, another experiment was performed to determine whether smaller doses of acetarsone are also prophylactic. Immediately after infection, three rabbits were given per os 0.025 Gm. of acetarsone per kilogram of body weight, and one, 0.01 Gm. per kilogram. The

latter animal showed extensive edema and a large hard node with numerous spirochetes on the thirty-seventh day. On the fiftieth day one of the three that received 0.025 Gm. per kilogram showed hard, large nodes in both testes with numerous active spirochetes. So far the other two have not shown any manifestations of syphilis, but they are still under observation.

According to our experiments, there can be no doubt that acetarsone given per os possesses prophylactic properties; this is shown in table 4.

THE CURATIVE EFFECT OF ACETARSONE IN EXPERIMENTAL SYPHILIS IN RABBITS

Because of the lower toxicity of their preparation, Levaditi and Navarro-Martin [2] were the only investigators among those we have mentioned who were able to determine the curative dose of acetarsone in experimental syphilis in rabbits. They stated that in their experiments the spirochetes disappeared from chancres in from 1 to 2 days after stovarsol was given by mouth in a dose of 0.75 or 0.66 Gm. per kilogram, and that the lesions healed in from 4 to 8 days after a second dose.

Collier and Evers [3] cured several rabbits with syphilis by the use of stovarsol per os in doses of 0.18, 0.25, 0.28 (given in two doses: 0.1 and 0.18 Gm.) and 0.15 Gm. (given in two doses: 0.025 and 0.125 Gm.). The spirochetes disappeared from the lesions in from 5 to 6 days. With smaller doses a cure could not be obtained. In rabbits treated intravenously or subcutaneously with a dose of 0.2 Gm. per kilogram of the sodium salt of the original Ehrlich preparation, the spirochetes disappeared in from 2 to 3 days. It should be borne in mind, however, that the curative doses in these experiments were close to the maximum tolerated dose found by these authors.

Worms [5] was unable to effect a cure in rabbits infected with the Truffi strain and by the Reichsgesundheitsamt's strain by the oral administration of stovarsol or spirozid in doses of 0.25 and 0.33 Gm. per kilogram. On the other hand, in animals inoculated with the Nichols strain, an apparent cure resulted from doses of from 0.17 to 0.25 Gm. in eight cases, while two animals that received 0.23 Gm. per kilogram were not cured. However, no definite conclusions could be drawn from these results, since most of the animals, except two that remained free from syphilitic lesions during two and five months, respectively, died after having been observed for two or three weeks.

Poole [6] gave 0.5 Gm. of stovarsol per kilogram by mouth to six rabbits displaying syphilitic orchitis. The animals died of drug intoxication within twenty-seven days. The popliteal lymph nodes and the testes of three rabbits were transferred to normal animals; no signs of

syphilis were seen during ninety days of observation. The lymph nodes of the other animals were not removed because of advanced postmortem changes.

The following experiments were performed in order to determine the curative effect of acetarsone prepared by us.

Rabbit 199, with well developed syphilitic lesions, was given six doses of the drug per os in a dosage of 0.05 Gm. per kilogram in the course of 11 days. The treatment was then interrupted, since the animal

TABLE 5.—*Treatment of Syphilitic Rabbits with Acetarsone*

	Syphilitic Manifestations Before Treatment				Treatment			Results Following Treatment		Popliteal Node Transfer	
			Dark-field Examination								
Number of Rabbit	Right Testis	Left Testis	Right Testis	Left Testis	Dose, Mg. per Kilogram of Body Weight	Frequency and Number of Treatments	Method of Administration	Tests	Dark-field Examination	Time of Transfer	Results of Transfer
199	Large and hard node	Large and hard node	+4,* very active	+4, very active	50	10 doses†	Per os	Normal after 60 days	Negative after 10 days	After 167 days of observation	Negative for 112 days
216	Large and hard node	Large and hard node	+4, very active	+4, very active	50	10 weekly treatments	Intravenous	Normal after 96 days	Negative after 32 days	After 209 days of observation	Negative for 112 days
2265	Large chancre; large, hard node	Large chancre; large, hard node	+4, very active	+4, very active	50	10 weekly treatments	Intravenous	Normal after 45 days	Negative after 25 days	Still under observation 160 days	
2266	Large and hard node; edema	Medium chancre; large and hard node	+4, very active	+4, very active	50	10 weekly treatments	Intravenous	Normal after 39 days	Negative after 16 days	After 120 days of observation	Negative for 50 days

* +4 indicates that the spirochetes are numerous.
† Six doses were given every other day. The other four doses were given after thirty-two days because the rabbit was losing weight.

was losing weight. The treatment was resumed 32 days later, and four weekly doses of 0.05 Gm. were given. No relapse occurred during 167 days of observation, and the popliteal nodes of rabbit 199 were then transferred to two normal animals; these animals remained entirely normal during the 112 days of observation. It appears from this that the treatment, consisting of ten repeated doses of 0.05 Gm. of acetarsone, was effective.

Rabbit 216, with large syphilitic lesions, received ten weekly doses of 0.5 Gm. of acetarsone, intravenously. The spirochetes disappeared on the thirty-second day, and the rabbit became normal after 96 days.

The animal remained under observation for 209 days, at the end of which time the popliteal nodes were removed. The transfer animals were observed for 112 days, they remained entirely normal.

Recently, two more syphilitic rabbits, 2266 and 2265, received intravenously ten weekly treatments, the same dose being used. The spirochetes disappeared from the lesions in from 10 to 25 days, and the testicles became normal in from 34 to 60 days. After 120 days of observation, the popliteal nodes of rabbit 2266 were transferred to two normal rabbits. These animals have remained normal, and are still under observation. Rabbit 2265 is likewise under observation, having remained normal for 160 days. These results are summarized in table 5.

THE PENETRATION OF ACETARSONE INTO THE CENTRAL NERVOUS SYSTEM

It has been shown by one of us (Dr. Raiziss) and Gavron [13] that pentavalent arsenicals penetrate the membranes of animals with much greater facility than compounds of the trivalent group, which are colloidal. Hence the penetrating power of the trivalent group is in general inferior to that of the pentavalent arsenical compounds.

Stovarsol belongs to the pentavalent group; it was one of the compounds the penetration of which into the cerebrospinal system formed the subject of a recent study that we made.[14] A biologic method was used in which trypanosomes or spirochetes were introduced into the cerebrospinal canal of rabbits which were treated two hours later with arsenicals, administered intravenously or by mouth. When trypanosomes were used, the spinal fluid was removed at various intervals and examined microscopically for these organisms. In their absence, rats were infected intraperitoneally with the spinal fluid, and the blood of the animals was examined every few days for a period of three weeks. If the spinal fluid did not contain trypanosomes, the rat survived; if trypanosomes appeared in its blood, it died in a short time. As shown in table 6, six rabbits that had been infected with trypanosomes injected intraspinally received acetarsone intravenously in doses ranging from 0.08 to 0.15 Gm. In only one of the six cases were trypanosomes absent both in the smears and in the blood of rats infected with the spinal fluid. Trypanosomes were present either in the spinal fluid or in the blood of rats infected with the spinal fluid of the other five rabbits. However, in this experiment no conclusions regarding the penetration of

13. Raiziss, G. W., and Gavron, J. L.: A Study of the Colloidal Properties of Arsphenamine and Allied Products, J. Pharmacol. & Exper. Therap. **20**:163 (Oct.) 1922.

14. Raiziss and Severac: Chemotherapeutic Studies Concerning the Penetration of Organic Compounds of Arsenic into the Cerebrospinal System, Arch. Dermat. & Syph. **22**:1031 (Dec.) 1930.

acetarsone into the cerebrospinal system could be made, for the two following reasons: 1. As pointed out by us and by others, acetarsone does not possess strong trypanocidal action. 2. Acetarsone is more effective when given per os, probably because of the slower elimination from the body than in intravenous administration.

From table 7, it is seen that when a dose of 1 Gm. of acetarsone was given per os and the spinal fluid examined forty-eight or more hours later, permanent sterilization resulted. Clearly, penetration of acetarsone into the cerebrospinal system is indicated.

TABLE 6.—*Acetarsone (Stovarsol) Given Intravenously to Rabbits Infected Intraspinally with Trypanosomes* *

Number of Animals Used	Dose per Kilogram of Body Weight	Microscopic Examination of Spinal Fluid 24 Hours Later	Weeks of Observation of Rats after Intraperitoneal Injection of the Spinal Fluid of Rabbits		
			1	2	3
1	0.080	—	+	D	
2	0.100	—	—	—	—
1	0.100	+			
1	0.120	—	—	+	D
1	0.150	—	—	+	D

* The acetarsone was suspended in water and alkalinized.

TABLE 7.—*Oral Administration of Acetarsone (Stovarsol) to Rabbits Infected Intraspinally with Trypanosomes*

Number of Animals Used	Dose per Kilogram of Body Weight, Gm.	Microscopic Examination of the Spinal Fluid After				Weeks of Observation of Rats After Intraperitoneal Injection of Spinal Fluid of Rabbits		
		24 Hours	48 Hours	5 days	7 Days	1	2	3
1	0.500	—	..	..	..	+	D	
1	0.500	..	—	..	..	—	+	D
1	0.500	..	..	..	—	+	D	
1	0.750	..	—	..	..	+	D	
2	0.750	..	..	..	—	—	—	—
1	1	+						
2	1	..	—	..	..	—	—	—
1	1	..	..	—	..	—	—	—
1	1	..	..	..	—	—	—	—

Interesting results were obtained when rabbits were infected intraspinally with Spirochaeta pallida and two hours later treated intravenously with acetarsone. If the compound used does not penetrate into the spinal canal and destroy the spirochetes in situ, scrotal, testicular or generalized lesions develop from two to four months after infection. Table 8 shows that stovarsol possesses a certain penetrative power. For instance, in rabbit 779, which received 100 mg. of acetarsone per kilogram intravenously, no lesions developed for a period of five months. Two rabbits inoculated with its popliteal nodes remained normal during eight months of observation. Another rabbit, which had received 0.050 Gm. per kilogram, remained normal during the entire period of

observation, forty-five weeks; the rabbits inoculated with its popliteal nodes have been normal for more than three months.

In two other rabbits that received intravenously 0.05 and 0.025 Gm. of acetarsone per kilogram, respectively, no lesions have developed during 150 days after infection and treatment; they are still under observation. These results are summarized in table 8.

Therefore, it is our opinion that the use of acetarsone in the treatment for neurosyphilis deserves the attention of syphilologists. In this connection, it is of interest to note that stovarsol has been used by Sézary and Barbé [15] in dementia paralytica, with rather favorable results.

Quite recently, Horster [16] reported experiments which indicate that the syphilitic infection of the central nervous system of mice, first

TABLE 8.—*Treatment of Rabbits with Intravenous Administration of Acetarsone Two Hours After Intraspinal Infection with Spirochaeta Pallida*

Rabbit No.	Dose per Kilogram of Body Weight, Gm.	Clinical Observation				Popliteal Node Transfer
		Right Testis	Left Testis	Generalized Lesions	Dark-field Examination	
779	0.10	Normal for 5 months	Normal for 5 months	.....	.....	Two normal rabbits inoculated with popliteal nodes of rabbit 779 remained normal during 8 months of observation
2092	0.10	Normal for 8 weeks	Normal for 8 weeks	.....	.....	Died on the sixtieth day
2090	0.05	Normal for 45 weeks	Normal for 45 weeks	.....	.....	Transfer animals remained normal during 3½ months of observation
2318	0.05	Normal for 26 weeks	Normal for 26 weeks	.....	.....	
2317	0.025	Normal for 26 weeks	Normal for 26 weeks	.....	.....	

demonstrated by Kolle, can be effectively dealt with by means of oral treatment with acetarsone.

CONCLUSIONS

1. The lower toxicity of acetarsone observed by us, as compared with the results of other investigators, is probably due to the greater chemical purity of the compound that we prepared.

2. Acetarsone has little effect in experimental trypanosomiasis.

15. Sézary, A., and Barbé, A.: Résultats cliniques et biologiques de la stovarsolthérapise dans 125 cas de paralysie générale, Presse méd. **37**:1 (Jan. 2) 1929; abstr., J. Chemotherapy **6**:15 (April) 1929.

16. Horster, H.: Tierexperimentelle Untersuchungen über die Wirksamkeit von Spirozid gegenüber der luetischen Infektion des Zentralnervensystems, Med. Klin. **27**:511 (April 2) 1931.

3. This drug when given to syphilitic rabbits per os possesses prophylactic properties.

4. Acetarsone has some curative action in experimental syphilis in rabbits.

5. Acetarsone is capable of penetration into the central nervous system, and should, therefore, be considered as a possible remedy in neurosyphilis.

A. Koppelman and J. C. Moetsch of the Dermatological Research Laboratories, Philadelphia, cooperated with us in this work.

EPIDERMOPHYTIDS AS A CLINICAL CONCEPTION

MOSES SCHOLTZ, M.D.
LOS ANGELES

Trichophytid as a clinical conception was first introduced in 1908 by Jadassohn,[1] who described lichen-like lesions on the trunk in patients with trichophytic kerion lesions on the scalp. These were associated with systemic symptoms and with a positive reaction to trichophytin. Later Bloch [2] confirmed and elaborated this conception on an immunologic basis by reproducing the condition experimentally by injections of trichophytin. He also described other types of lesions, such as scarlatinoid, erythema multiforme, nodular and pustular. Several other observers, among them Brash, reported similar lesions and supplied more immunologic evidence. Sutter [3] demonstrated fungi in lymphatic glands, and Bruusgaard [4] found fungi in the sections of small veins. All these studies, however, were made in cases of deep trichophytosis, mostly of kerion type.

In 1911 Sabouraud [5] for the first time isolated epidermophyton fungus from the superficial eczematoid vesicular and scaly intertriginous lesions of the toes. This began a new series of bacteriologic studies which have established the clinical entity of mycotic dyshidrosis of the hands and feet.

Wolff,[6] Mitchell and Ormsby,[7] Chrameck, Darier,[8] White [9] and others found and cultivated fungi from so many dyshidrotic lesions that it became popular to deny the systemic origin of dyshidrosis, as originally suggested by Tilbury Fox, and to consider all of the lesions mycotic. Peculiarly several clinicians have lately reported many negative

---

Submitted for publication, June 1, 1931.

From the department of Dermatology, College of Medical Evangelists and Los Angeles General Hospital.

1. Jadassohn, J.: Klin. Wchnschr., 1918, p. 489.
2. Bloch, Bruno: Ann. de dermat. et syph. **2**:1, 1921.
3. Sutter: Arch. f. Dermat. u. Syph. **127**:735, 1919.
4. Bruusgaard, E.: Brit. J. Dermat. **34**:150 (May) 1922.
5. Sabouraud, R.: Ann. de dermat. et syph. **1**:289, 1910.
6. Wolff, Kauffman: Dermat. Ztschr. **20**:385, 1914.
7. Ormsby, O. S., and Mitchell, J. H.: Ringworm of Hands and Feet, J. A. M. A. **67**:711 (Sept. 2) 1916.
8. Darier, J.: Lancet **2**:578, 1919; Précis de dermatologie, Paris, Masson & Cie, 1927.
9. White, Charles, and Greenwood, A. M.: Epidermophytosis, Tr. Sect. Dermat. & Syph., A. M. A., 1921, p. 181.

microscopic observations and cultural findings in the clinically apparently mycotic lesions on the hands and positive findings from the lesions on the feet.

To explain this apparent clinical discrepancy, Williams [10] of New York suggested that the lesions of the hand may be regarded as trichophytids due to the absorption of the fungi toxins from the lesions of the feet. This idea was followed and elaborated by Bruno Bloch and his school. W. Jadassohn and Peck [11] published thorough bacteriologic and experimental studies of a series of cases of dyshidrotic and scaly mycotic lesions of the hands and feet. On the strength of these studies, they established a clinical entity of palmar and digital epidermophytids and trichophytids, or briefly "ids."

The main emphasis and argumentation advanced in behalf of the palmar and digital "ids" was centered on bacteriologic, experimental and immunologic observations. The clinical interpretation of the phenomenon was not attempted or was omitted possibly because the authors were primarily absorbed in the experimental and allergic angle of the problem. However, since the conception of epidermophytid was brought into existence primarily to explain a certain clinical phenomenon, it cannot be accepted on the laboratory evidence alone, without clinical interpretation and correlation with clinical data. To supply this clinical interpretation and to analyze the problem from a clinical point of view is the purpose of this paper.

To recapitulate the definition of the palmar and digital epidermophytids as postulated by Peck of the Bloch school: The condition is toxic lesions caused by hematogenously deposited fungi or their toxins from the lesions on the feet. As a rule, the lesions are negative bacteriologically, microscopically and culturally, but give a positive trichophytic reaction. They can be reproduced experimentally.

BACTERIOLOGIC FINDINGS

The basic bacteriologic evidence advanced by Peck and W. Jadassohn in support of the conception of palmar and digital epidermophytids is the uniformly negative fungi findings in the lesions of the hands while the lesions of the feet were constantly positive for fungi. However, these findings are in conflict with those of other observers.

---

10. Williams, Charles: Dermatophytid Complicating Tursa Cruris, Arch. Dermat. & Syph. **22**:636 (Oct.) 1930; Tinea Barbae Involving Upper Lips and Accompanied by Dermatophytid, ibid. **23**:213 (Feb.) 1931.

11. Jadassohn, W., and Peck, S.: Epidermophytosis of the Feet and Epidermophytids of the Hands, Arch. Dermat. & Syph. **22**:40 (July) 1930; Arch. f. Dermat. u. Syph. **158**:16, 1929.

Sicoli,[12] working in Sabouraud's laboratory, reported a series of 113 cases of palmar dyshidrosis, in 47 of which he demonstrated fungi and in 64 of which he failed to find them; 38 of these he regarded as cases of pseudodyshidrosis and 28 as cases of true dyshidrosis.

Mitchell and Ormsby[7] in 1916 reported a series of 65 cases of dyshidrosis of the hands and feet with positive fungi findings in all cases, which led them to the conclusion that dyshidrosis is often of mycotic origin. Darier in 1919 studied bacteriologically a large series of cases of dyshidrosis of the hands and feet. He demonstrated fungi in 11 of 14 cases occurring on the hands and in 6 out of 11 occurring on the feet.

C. J. White of Boston, in 1927, in a study of a series of cases of epidermophytosis, observed fungi microscopically in 5 of 10 cases of lesions on the hands and in 7 of 11 in which the lesions were on the feet and obtained a culture in 2 of 15 cases of lesions on the hands and in 3 of 11 cases of lesions on the feet.

At the congress of Swiss Dermatologists in 1929, no less an authority in clinical mycology than Sabouraud questioned the validity of uniformly negative fungi findings in the lesions of the hands by Peck and W. Jadassohn. This discrepancy in the basic bacteriologic findings presents the first weak link in the chain of evidence advanced in support of the conception of palmar and digital epidermophytids.

ALLERGY AND THE TRICHOPHYTON TEST

Allergic evidence in support of the conception of the palmar and digital epidermophytids consists of the positive fungi blood culture and positive results of trichophyton tests. However, the positive blood culture, owing to technical difficulties and low viability of the fungus in living blood, has been reported as an exceptional result. In fact, Peck found it in only 1 case of a series of 26. Pellizaro obtained it only in 1 of 700 specimens of blood.

This exceptional incidence of positive results renders the criterion of blood culture a test of scientific interest, illustrating an allergic pathogenesis of trichophytids rather than furnishing concrete evidence of the validity of the conception.

A positive trichophyton test is stressed as an important link of allergic evidence in establishing a clinical entity of palmar and digital epidermophytids.

The argumentative weight of the results of this test would be irrefutable and conclusive if the test should be specific. But its specificity is not generally accepted, and is disputed by many.

---

12. Sicoli, A.: Ann. de dermat. et syph. **5**:69, 1924.

J. Jadassohn [13] regarded it as a "relatively crude test," and Mitchell as unreliable. Arnold,[14] in a study on children, found so many positive reactions in healthy subjects that he considered the test of little diagnostic value. Sloimovici and Ullmo [15] found that the reactions to intradermal injections of trichophytin were specific for deep trichophytosis but rather inconstant in superficial cases. Darier granted some diagnostic value to the trichophyton test, but stated that positive reactions occur also in healthy subjects. Ravaut [16] found positive reactions in the lesions caused by the yeast cells. Finally, Bloch himself stated that a positive trichophyton test does not necessarily mean that the skin lesions are caused by fungi or their toxins, but rather that the patient has had trichophytosis infection. According to Bloch, a positive reaction to trichophytin may persist for a long time after clinical symptoms of epidermomycosis have completely disappeared. This persistent nature of the trichophytin reaction detracts from its clinical value and contributes to the vagueness and uncertainty of clinical deductions from it, as it allows the assumption of palmar and digital epidermophytids in the absence of demonstrable lesions of the feet.

PERSONAL SERIES

My personal experience with the trichophyton test is limited to a series of 28 cases. The testing was done intradermally by my associate, Dr. Charles R. Caskey. Commercial trichophytin was used with its diluent as a control. The control in all cases except 1 was negative.

This series comprised 7 cases of dyshidrotic lesions on the hands only, 4 on the hands and feet, 4 in the groins and on the feet, 7 on the feet only and 1 in the axilla only. In 6 cases there were no mycotic lesions.

In 24 cases the trichophyton test gave a positive reaction and in 4 cases the reaction was negative. Among the positive cases, the reaction in one half was very pronounced, and in a few of these there was aggravation of the local lesions. The reaction in the other half was moderately or weakly positive. In 7 cases there were no visible, or only very faint, lesions on the feet. In a case in which there were lesions on both the feet and the hands all lesions began to improve promptly under treatment with fungicidal ointment. Then the hands were treated with bland boric acid ointment, while the former treatment was continued on the feet; the feet continued to make steady improvement, while on the hands crops of fresh dyshidrotic lesions developed.

13. Jadassohn J.: Importance of Immune Biologic Processes in Morphology of Skin Lesions, Arch. Dermat. & Syph. **21**:355 (March) 1930.

14. Arnold: Arch. f. Dermat. u. Syph. **136**:225, 1923.

15. Sloimovici, M. A., and Ullmo, A.: Ann. de dermat. et syph. **8**:554, 1927.

16. Ravaut: Presse méd. **36**:1443 (Nov. 14) 1928.

The impression gathered from this limited series is that the trichophyton test is conducive to false positive reactions and is not very selective in action. The frequent positivity of reaction of patients who have or have had even mild and superficial mycotic lesions of the feet without any other lesions elsewhere detracts considerably from the allergic significance of the test.

Considering the unproved specificity of the trichophyton test, it can be granted only relative and circumstantial value in the diagnosis of epidermophytids.

EXPERIMENTAL REPRODUCTION OF DYSHIDROSIS

The experimental reproduction of the dyshidrotic lesions seems to be the strongest link in the chain of evidence so far presented in support of the conception of the palmar and digital epidermophytids. It must be accepted as an irrefutable proof of the capacity of trichotoxins to produce clinically dyshidrotic lesions, but obviously it does not prove that all palmar and digital dyshidrotic lesions that happen to be coincidental with similar lesions on the feet are due to trichophytic toxins, that is, are epidermophytids.

PALMAR AND DIGITAL EPIDERMOPHYTIDS CONSIDERED CLINICALLY

The general conception of trichophytids introduced by J. Jadassohn and elaborated by Bloch is so rational and plausible from the point of view of the clinician that it can readily be accepted by him. This conception conforms fully and in all details with clinical experience and does not raise any unsolved problems. On the other hand, the conception of palmar and digital epidermophytids advanced by Peck and W. Jadassohn, while presenting bacteriologic evidence well worked out, and suggestive if not conclusive, raises from the clinical point of view so many unsolved problems and questions that it can hardly be accepted without further clinical elucidation. To start with, palmar and digital epidermophytids differ radically from any heretofore described trichophytids, both in morphology and in clinical behavior. The types of trichophytids described so far are lichenoid, follicular, spinulous scarlatinoid, erythematous, erythema multiforme, nodular and pustular. Dyshidrotic, squamous types identical with the primary mycotic lesions have never been described. The trichophytids are usually described as acute lesions developing suddenly on multiple points of location and just as rapidly clearing up. Palmar and digital dyshidrotic and squamous lesions following those on the feet in many cases develop on one hand only, from one patch, spread by extension and show marginal activity. In other words, the palmar lesions mimic not only the morphology, but also the clinical behavior of the primary mycotic lesions of the feet.

Granting even, as it has been assumed by Charles Williams of New York, that the morphology of the mycotic lesions is determined by the combined effects of the living fungi and their toxins, and that toxins alone can produce lesions similar or identical to those produced by living fungi, it remains clinically inconceivable and unexplainable that the lesions produced by the toxins alone could mimic completely the clinical behavior, mode of development, extension and involution of the lesions produced by living fungi. Yet this is what is claimed for the palmar and digital epidermophytids.

None of the trichophytids so far described show such a tendency both to resistance to all kinds of treatments and to recurrences. This fact, which is confirmed by common dermatologic experience, conflicts with Peck's statement that palmar and digital epidermophytids clear up without local treatments after the primary lesions on the feet clear up. This clinical fact, which was also accepted by Williams, the originator of the idea of palmar "ids," and well emphasized by Mitchell, conflicts with the original conception of Bloch that trichophytids work out an immunity, are never chronic and do not recur. In my experience the lesions in cases of palmar epidermomycosis are at least as persistent as those in plantar epidermomycosis and often more so.

Does Peck deny the possibility of primary mycotic infection on the hands? Such cases are within common dermatologic experience. And if this contingency is admitted, how can one refute the possibility and likelihood of ectogenous transference of fungi from the feet to the hands?

The fact of the usual sequence of the development of the mycotic lesions of epidermophytids first on the feet and then on the hands, so much stressed as an argument for their hematogenous origin, can be just as naturally explained by the fact that the feet are the usual and most favorable habitat medium for the primary mycotic infection.

Moreover, the opportunities for self-inoculation and transference of the fungi from the feet to the hands in daily life are so numerous that it is more natural to conceive that the lesions of the hands are of ectogenous origin than to assume that there is a peculiar constant selection of the hands by toxins circulating throughout the whole system. And how would protagonists of the palmar epidermophytids interpret dyshidrotic lesions limited to the hands only, lesions that at present are regarded either as primary mycosis or as true pompholyx?

Among many clinical problems raised by the conception of the palmar and digital epidermophytids that remain unsolved and unexplained is the absorption of trichophytic toxins from the apparently dry and extremely superficial lesions on the feet. This fact stands rather in sharp contrast with all previous descriptions of trichophytids, which were observed invariably in deep pyogenic trichophytic lesions.

In contrast with this singular absorbability of toxins from dry and superficial lesions stands the remarkable scarcity of clinical observations of toxic eruptions due to absorption from the superficial dermatoses caused by pyogenic bacteria or yeast cells, lesions that commonly present large, weepy exudative surfaces, apparently conducive to absorption. So far only one writer, Ravaut, has reported an observation suggesting the possibility of such eruptions, which he calls "streptococcides and levurides."

One of the confusing points in the conception of epidermophytids is the finding of fungi in the palmar and digital lesions. While claiming negative findings in an overwhelming majority of cases, Peck and W. Jadassohn do admit positive findings in a few cases. Other observers claim a much larger percentage of positive findings. Apparently to rectify this conflicting and puzzling factor, J. Jadassohn has created a concept of ectogenous trichophytid implying that fungi locate and become pathogenic only after the trichophytic toxins hematogenously deposited have sensitized the skin and rendered it allergic. Bloch rejects this conception and accepts the endogenous route as the most likely.

In my opinion the conception of ectogenous trichophytids, instead of clarifying the question, renders it still more complicated and confused, and makes still more difficult the differentiation of this condition from conditions caused by direct transference of fungi and self-inoculation from the lesions on the feet.

Williams goes still further and advances an original but extreme idea that even some of the lesions on the feet (those in which fungi cannot be demonstrated) are epidermophytids while the others are true mycotic lesions. Should this assumption be proved correct, the conception of epidermophytids would retain only theoretical significance, as practical evaluation and clinical diagnosis would be virtually impossible and any clinical deductions would be out of question.

The important practical deduction drawn from the conception of epidermophytids that the lesions on the hands do not require active local medication as, according to Peck's observation, they clear up spontaneously after the primary mycotic lesions on the feet disappear cannot be accepted, since this observation is not supported by daily clinical experience.

TRUE DYSHIDROSIS VERSUS MYCOTIC DYSHIDROSIS

One of the important implications in the acceptance of the concept of palmar and digital trichophytids is the denial of the existence of true systemic dyshidrosis or pompholyx of Tilbury Fox as a clinical entity. The controversy on dyshidrosis has been waging almost from the very

inception of the original conception of Fox that it was due to a disturbance of the sweat glands. This idea was upheld fully by Crocker and partly by Hutchinson, and was opposed on histopathologic grounds by Hutchinson, Robinson, Williams, Santi and Sutton. Unna described a germ as an etiologic factor in dyshidrosis, but it has never been found by others.

Darier, in 1919, on the strength of his bacteriologic findings proclaimed that dyshidrosis is a mycotic condition. This report gave rise to a widespread tendency to deny the clinical entity of the systemic dyshidrosis of Fox and to regard the lesions as mycotic even in the face of negative fungi findings. Only a few clinicians had the courage to oppose this view. Among these are to be mentioned Sabouraud and his school, Sicoli, Ravalier and Pereira, who accept three types of dyshidrosis: mycotic dyshidrosis, pseudodyshidrosis, that is vesicular eczema, and true dyshidrosis.

At the congress of French speaking dermatologists in 1929, half of the members accepted true systemic dyshidrosis and half of them did not. Whitfield of England also believed in true dyshidrosis. On the other hand, Bloch and his school strongly uphold the mycotic nature of dyshidrosis.

Several German observers also accept the clinical entity of true systemic dyshidrosis, as Alexander,[17] Raika,[18] Keller[19] and Karrenberg.[20]

A large number of American dermatologists still believe in the systemic origin of dyshidrosis; among these are Ormsby,[21] Wile, Fred Wise, Grindon, O'Leary,[22] Sutton and Lehmann.[23] On the other hand Williams, Hazen and Highman regard the condition as mycotic.

The idea that dyshidrosis may be produced by pyogenic microorganisms from the focal infection has been reemphasized lately by E. Kenery.[24]

CLINICAL DIFFERENTIATION

The diagnostic value of the morphologic differentiation between mycotic dyshidrotic lesions and those of systemic dyshidrosis has been generally underestimated by dermatologists and completely ignored by

17. Alexander, A.: Dermat. Ztschr. **50**:185, 1927.
18. Raika: Arch. f. Dermat. u. Syph. **143**:205, 1928.
19. Keller, P.: Dermat. Ztschr. **49**:33, 1926.
20. Karrenberg, C. L.: Inquiries into the Present State of Epidermophytids in Europe, Tr. Sect. Dermat. & Syph., A. M. A., 1927, p. 179.
21. Ormsby: Treatise of the Diseases of the Skin, Philadelphia, Lea & Febiger, 1921.
22. Sutton: Diseases of the Skin, St. Louis, C. V. Mosby Company, 1926.
23. Lehmann, C. F.: Acute Vesicular Eruptions of Hands and Feet, Arch. Dermat. & Syph. **21**:449 (March) 1930.
24. Kenery, L.: Dermat. Wchnschr. **43**:1577, 1930.

the protagonists of epidermophytids. Granting even that a few borderline cases may present some confusion and overlapping of morphologic features, this confusion is more apparent than real and occurs only if one is guided by the general pictorial design of the lesions without using a systematic analysis and differentiation of morphologic details. It is a peculiar and rather conflicting fact that the systemic nonmycotic nature of true dyshidrosis was denied first by Darier, Mitchell and others because of the numerous positive fungi findings in dyshidrotic lesions of the hand and is denied at present by the protagonists of epidermophytids on the opposite claim of the negative findings.

The following morphologic traits seem to be accepted by clinicians as clinical characteristics of vesicular epidermophytosis: Mycotic vesicles, deep or superficial, often inflammatory though only mildly, mostly small, usually not uniform in size, exhibit a tendency toward clustering or grouping and spreading by periphery, forming circinate or polycyclic edges showing marginal activity and an epidermal collarette. Mycotic vesicles usually rupture early by scratching, and on drying up change into the squamous type. Commonly one can see patches and individual lesions in various stages of development.

Ordinarily the onset is gradual, the course is resistant, and there is a tendency to recurrence. Moreover, the location of the primary mycotic lesions is variable (though the third and fourth interdigital spaces on the feet seem to be sites of predilection). Mycotic dyshidrosis is often bilateral but seldom symmetrical in distribution.

On the other hand, true systemic dyshidrosis is characterized by deep, uniform, noninflammatory, sago grain-like vesicles, which spring up in dozens or hundreds simultaneously on various parts of the palms and fingers, burning rather than itching. These vesicles seldom rupture spontaneously and are seldom scratched open because of the lack of itching. They may coalesce into large bullae and undergo pyogenic infection. In small vesicular types they dry up in a few days by absorption and disappear with light desquamation. The vesicles do not show a tendency to form circinate or polycyclic rows or clusters. The desquamation is not of the type of the familiar epidermal collarette, but presents a scarlet fever type throughout the whole depth of the skin in irregularly shaped flakes, patches and large fragments of skin in toto. The vesicles are as a rule symmetrical, develop suddenly and cover large areas at once.

This detailed morphologic differentiation, if applied in a systematic and thorough manner, will effect clinical differentiation in a majority of cases.

Still less, in my opinion, should there be any occasion for the confusion of the morphologic pictures of mycotic dyshidrotic lesions and vesicular occupational eczemas. Eczematous vesicles, in contra-

distinction to the mycotic ones that were portrayed, are, as a rule, small, superficial and never discrete; they invariably coalesce into irregular ill defined patches with an infiltrated base and weepy surface. This tendency of eczematous vesicles to a serous exudation in contradistinction to mycotic vesicles which dry up quickly, forming the turned-up, attached scaly edges of the epidermic collarette, was noticed and emphasized by Wolff in her original report of 1914. It is true that mycotic dyshidrosis often leads to secondary eczematization, which leads to borderline cases of mixed morphology, but even in these cases, the clinical earmarks of the underlying primary mycosis are readily detected by careful morphologic differentiation. True dyshidrosis, in my experience, seldom produces secondary eczematization and continues throughout the course as a toxic rash.

It is hard to see a resemblance between the noninflammatory, unruptured, uniform, discrete sago grain-like vesicles and bullae of true dyshidrosis and the small superficial, inflammatory, confluent, scratched open eczematous vesicles. Neither does there seem to be much resemblance between the scarlet fever type of exfoliation of the true dyshidrosis and the small irregular eczematous scales, often heaped up and firmly attached to the infiltrated inflammatory eczematous base. Speaking generally, a detailed morphologic differentiation can establish the clinical diagnosis of these dermatoses in a majority of cases in spite of a general resemblance of their clinical pictures.

The statement that clinical differentiation between mycotic and nonmycotic dermatoses cannot be made without bacteriologic confirmation, although perhaps theoretically correct, seems to me to be too extreme and not sustained by clinical experience. This opinion is held by many clinicians, among them Sabouraud and C. H. White.

CONCLUSIONS

In summarizing the analysis of the clinical concept of the palmar and digital epidermophytids the following points can be emphasized:

1. The bacteriologic evidence presented cannot be accepted as conclusive, because the claim of uniformly negative findings in the lesions of the hand is not concurred in by other observers.

2. The trichophyton test is not specific, and because of its persistent nature is conducive to false positive tests and vague and uncertain clinical deductions.

3. Positive blood cultures and the experimental reproduction of mycotic dyshidrotic lesions are of argumentative importance, but so far they have been found positive in so few isolated cases as hardly to be definite proof of the conception of epidermophytids.

4. From a clinical point of view the conception of palmar and digital epidermophytids gives rise to many unsolved questions and unexplainable clinical problems; it rests also on statements and observations so conflicting with general dermatologic experience as to render it inacceptable without further clinical elucidation.

SUMMARY

A clinical analysis of the conception of epidermophytids is offered. A series of twenty-eight cases in which intradermal injections of trichophytin were made is presented.

URTICARIA FROM SENSITIVENESS TO COLD

RECOVERY FOLLOWING REMOVAL OF A PELVIC TUMOR

EDWARD WEISS, M.D.
Associate in Medicine, Jefferson Medical College
PHILADELPHIA

REPORT OF A CASE

Mrs. F. S., a Jewess, aged 39, was first seen in August, 1925, when she complained of hives of seven weeks' duration.

The family history was negative for allergic disturbances. The past history revealed no serious illness. The menses were normal. The patient had never been pregnant. She had suffered from constipation as long as she could remember. She had been nervous for three months owing to domestic difficulties, which, however, had been satisfactorily settled.

General physical examination and examination of the urine and stools gave negative results. The blood count, blood sugar and blood urea nitrogen were normal. A dental x-ray film demonstrated an abscess of one tooth, which was extracted. Gynecologic examination revealed a fibroid tumor of the uterus, to which no great attention was paid at the time. A complete series of food tests (scratch method) was made, with no definite results. Colonic irrigations and acidophilus implantation did not benefit the hives. The patient, who lived out of the city, went home in September and returned the following February; she stated that at no time had she been free from hives. An important point, which she had mentioned before but now emphasized, was that contact with cold brought out the hives. Grasping a glass of cold water would produce hives on the hands; drinking cold water made her throat sore; sitting on a cold toilet seat produced hives on the buttocks, etc.

A piece of ice wrapped in a towel was applied to various parts of the body. A moment's application was followed by redness, itching and a typical urticarial wheal. Treatment with calcium and with parathormone was attempted without results, and bathing with water at decreasing temperatures was advised in an effort to desensitize the patient to cold.

The patient was not seen from January, 1927, until August, 1928. She reported that she had had no severe hives during that time, but that she had remained sensitive to cold as previously described. In addition, she complained of cramplike pains in the lower part of the abdomen, and a tender mass was palpated. An abdominal operation was done, and a large fibroid tumor of the uterus, which pressed on and was attached to the sigmoid colon, was removed. The patient made a good recovery, left the city and was not heard from until one year later, in August, 1929. She then stated that she had had no hives since the operation and was able to take cold showers without trouble. She could even handle ice, the only sensation being a slight itching in the palms. A report in January, 1931, stated that she no longer had hives, nor was she bothered by cold. Physical examination and laboratory studies showed that she was in excellent condition.

Submitted for publication, July 27, 1931.

COMMENT

This case apparently corresponds to those described by Duke and others (Horton and Brown [1] and Blackford [2]) as presenting a state of physical allergy with sensitiveness to cold. It is difficult to be certain that the removal of the large pelvic tumor that pressed on the bowel and that in all probability was an important factor in the long history of constipation was responsible for the cure of the condition. The patient had made some improvement prior to the operation, and it is possible that her recovery from sensitiveness to cold would have taken place without operation. However, the difference in her reactions before and after operation was striking. No attempt is made at explanation. Remarkable and often dramatic recoveries from allergic states after nonspecific treatment are too well known to merit further comment. The report of the case serves merely to emphasize that factors as yet poorly understood are fundamental in such disorders.[3]

1. Horton, B. T., and Brown, S. E.: Am. J. M. Sc. **178**:191, 1929.

2. Blackford, L. M.: Cold Urticaria and Histamine Allergy; Report of a Case, J. A. M. A. **96**:525 (Feb. 14) 1931.

3. Weiss, E.: J. Allergy, to be published.

THE REACTION OF THE SKIN AND ITS SECRETIONS IN ECZEMA

I. THE HYDROGEN ION CONCENTRATION OF THE SKIN SURFACE IN ECZEMA

OSCAR L. LEVIN, M.D.

Attending Dermatologist, Sea View and Beth Israel Hospitals; Associate Dermatologist, Mount Sinai and Montefiore Hospitals

AND

SEYMOUR H. SILVERS, M.D.

Adjunct Dermatologist, Beth Israel Hospital; Assistant Attending Dermatologist and Syphilologist, Bellevue Hospital and New York University Medical Clinic

NEW YORK

During the past few years, laboratory research in the physiology and chemistry of the skin has yielded important results. The close alliance between physiologic chemistry and clinical dermatology has been demonstrated, and it is probable that more knowledge of this alliance will have great influence in bringing about an understanding of various skin conditions that are now, for the most part, incomprehensible.

Investigators have been especially interested in the reaction and secretions of the skin in health and disease. It has been shown that an altered reaction affects the skin as a medium and may favor the growth and multiplication of saprophytic and pathogenic organisms. The result is naturally injurious and may even be accompanied by changes in the morphology of the skin cells. But it is difficult and at times impossible to determine when the changes in the reaction of the skin or skin surface are primary, causing the changes, or secondary, resulting from alteration of the cell architecture.

We have attempted here to determine the hydrogen ion concentration of the skin surface in eczema with a view to checking the efficiency of topical remedies.

REVIEW OF THE LITERATURE

The p_H of cells, blood and tissue juices has been investigated by various observers, the symbol p_H being used to indicate the hydrogen ion concentration of a solution. It is defined as the logarithm of the reciprocal of the H-ion concentration. When the hydrogen ions and

Submitted for publication, June 12, 1931.

From the Department of Dermatology, Beth Israel Hospital.

Read before the Section on Dermatology and Syphilology of the New York State Medical Society, Syracuse, N. Y., June 3, 1931.

the hydroxyl ions in a solution are equal, the p_H is 7 and the solution is neutral. A low p_H in a solution indicates a greater number of hydrogen ions and an increase in acidity. Figures over p_H 7 indicate alkalinity and an increase in the hydroxyl ions. The degree of alkalinity of a solution is indicated by the increase of the p_H over 7.

It has been determined that the normal reaction of any living cell is slightly acid. Michaelis and Kramstyk [1] placed the figure at 6.8, or just below neutral. The acidity increases when the cell is actively engaged in metabolism and its waste products are not carried away rapidly enough. The reaction of the blood is toward the alkaline side, the figures 7.35-7.4 being kept constant by means of buffers. The p_H of the tissue juices has been placed at 7.09-7.29, being between that of the blood and that of the cell. In diseases and inflammations the reaction of the cell and tissue juices becomes more acid. Schade, Neukirch and Halpert [2] investigated this particular phase and found that in inflammation the subcutaneous connective tissue showed a p_H of 5.6. This is decidedly acid.

The exact determination of the p_H of skin cells is much more difficult than that of the blood and tissue juices, owing to the buffer reaction of salts and albumin.

Unna and Golodetz [3] were among the first to investigate the reaction of the skin cell. They employed indicators and cut very thin layers of skin, noting that the reaction of the epidermal cells was acid, and became alkaline when the papillary bodies were reached. More recently, Rothman,[4] also employing an indicator, found that the epidermis gave an acid reaction and the cutis an alkaline reaction. Schmidtmann [5] used Peterfi's micromanipulator to study the reaction of the skin of animals. He injected an indicator intracellularly and as a result found that the epidermal cells reacted acid. The basal layer is most acid, the acidity gradually decreasing until the horny layer is reached. Here again the acidity becomes marked. The probable explanation of the greater acidity in the basal layer is that here, as in the case of inflammation, metab-

1. Michaelis, L., and Kramstyk, A.: Die Wasserstoffionenkonzentration der Gewebssäfte, Biol. Zentralbl. **62**:180, 1914.

2. Schade, H.; Neukirch, P., and Halpert, A.: Ueber lokale Acidose des Gewebes und die Methodik ihrer intravitalen Messung, Ztschr. f. d. ges. exper. Med. **24**:11, 1921.

3. Unna, P. G., and Golodetz, L.: Zur Chemie der Haut: VI. Hautreagenzien, Monatsh. f. prakt. Dermat. **50**:451, 1910.

4. Rothman, S.: Die aktuelle Reaktion der Haut, in Jadassohn: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1929, vol. 1, p. 325.

5. Schmidtmann, M.: Ueber die intracelluläre Wasserstoffionenkonzentration unter physiologischen und einigen pathologischen Bedingungen, Ztschr. f. d. ges. exper. Med. **45**:714, 1925.

olism is most active, producing more waste products and thereby serving to increase the acidity. In the succeeding cellular layers metabolism is slowed up, resulting in a somewhat decreased acidity. At the horny layer there is again a greater acidity, for here there are dead cells, which react strongly acid.

The p_H of water extracts of the skin has been investigated by Yamasaki,[6] who found it to be alkaline. He set the figure at 7.1-7.5. Hayashi [7] studied the p_H of skin extract of rabbits and obtained a lower figure, namely, 6.94-7.01. He also found that different food ingredients affect the hydrogen ion concentrates of the skin extracts. The p_H of eczema skin extracts was studied by Meineri.[8] The extracts showed a p_H of 7.33, a definitely alkaline reaction. Crosti [9] studied the p_H of the serum of artificial blebs produced by cantharides. In a normal subject the reaction of the serum was similar to that of the blood. In exudative and infiltrating dermatoses, the p_H of the serum was also similar to that of the blood. However, in the psoriasiform lesion, the p_H was relatively more acid than in the exudative eruption.

Bazett and McGlone [10] have studied the reaction of the skin in the following manner. They injected a dye intravenously and noticed the resulting color changes that took place in the skin that had been shaved. They found that as a result of irritation, such as that caused by shaving, there was an increase in the alkalinity. An increase in alkalinity was also observed to result from cooling. A change to the acid side was observed as the result of heating the skin or diminishing the blood supply. After prolonged interference with the blood supply, the increased acidity remained for from about five to ten minutes. In inflammation, they found an acid reaction surrounded by a hyperemic zone.

Liechti [11] and Kaplansky and Soloweitschik [12] found that when the roentgen rays are applied to the skin they tend to increase the acidity

6. Yamasaki, Y.: Ueber die Fermente der Haut, Biochem. Ztschr. **147**:203, 1924.

7. Hayashi, Hirokichi: Experimentelle Studien über die Empfindlichkeit der Haut gegen äussere Reize, Jap. J. M. Sc. Tr. Sect. XIII, Dermat. **1**:95, 1927; Zentralbl. f. Haut- u. Geschlechtskr. **34**:682, 1930.

8. Meineri, P. A.: Il p_H di estratti di cute eczematosa e psoriasica, Dermosifilografo **5**:73, 1930; Zentralbl. f. Haut- u. Geschlechtskr. **34**:682, 1930.

9. Crosti, A.: Ricerche su alcune proprietà fisico-chimiche del sangue e degli essudati cutanei in dermatosi, Gior. ital. di dermat. e sif. **70**:1063, 1929; Zentralbl. f. Haut- u. Geschlechtskr. **34**:682, 1930.

10. Bazett, H. C., and McGlone, B.: The Effect of Temperature on the Acidity of the Skin, J. Physiol. **64**:393, 1928.

11. Liechti, A.: Ueber Reaktionsänderungen im Röntgenstrahlen Gewebe, Klin. Wchnschr. **4**:1911, 1926.

12. Kaplansky, S., and Soloweitschik, S.: Ueber die Wirkung ultravioletter und Röntgenstrahlen auf die aktuelle Reaktion der Haut, Ztschr. f. d. ges. exper. Med. **55**:111, 1927.

of the tissue juices in the subcutis. By means of indicators, Gans [13] was able to show that the increase in acidity is only temporary, affecting mainly the basal cell layer and the endothelium of the capillaries, and that from two to twenty hours after irradiation, the p_H again tends toward the alkaline. Kaplansky and Soloweitschik also found that the H-ion concentration increased after the application of ultraviolet rays. Memmesheimer [14] made a study of the skin surface after the application of the roentgen rays. Twenty-four hours after irradiation, he found a decided tendency toward the alkaline, due, he believed, to an increase in the amount of blood supplied to the tissues and tissue juices. Keller [15] reported an increased p_H in erythema caused by ultraviolet irradiation.

On investigating the reaction of the skin surface that had been cleaned, using indicators, Sharlit and Scheer [16] found the p_H to equal about 5.5. This result was corroborated by Memmesheimer. Also working with indicators, Lloyd and his associates [17] have found that the intact stratum corneum is acid in reaction and has the ability to disinfect itself rapidly and efficiently. The disinfection against exogenous bacteria, such as B. coli, B. typhosus, B. prodigiosus, etc., is more complete than that against the endogenous staphylococci. Greasy substances on the skin inhibit the disinfecting property of the skin surface. In the region of the tips of the nails the disinfecting properties are very slight. To change the reaction of the skin surface to the alkaline side, Lloyd had to injure or destroy the horny layer of the epidermis.

One interesting problem that has received the attention of many investigators is the reaction of sweat. The figures of Talbert,[18] an early investigator in this field, have been corroborated lately by many other research workers. Talbert found that heat sweat has a p_H of 5.73 and work sweat a p_H of 6.4, evidently a fairly acid reaction. He also reported that the acidity of sweat from covered parts is slightly higher

13. Gans, O.: Ueber die biologische Wirkung und die Angriffspunkte der Röntgenstrahlen, Arch. f. Dermat. u. Syph. **155**:64, 1928.

14. Memmesheimer, A.: Die H-ion Konzentration der Hautoberfläche, Klin. Wchnschr. **3**:2102, 1924.

15. Keller, P.: Die biologischen Grundlagen für die elektrischen Potentiale der Haut, Arch. f. Dermat. u. Syph. **160**:136, 1930.

16. Sharlit, H., and Scheer, M.: The Hydrogen-Ion Concentration of the Surface of the Healthy Intact Skin, Arch. Dermat. & Syph. **7**:592 (May) 1923.

17. Lloyd, Arnold; Gustafson, C. J.; Hull, T. G.; Montgomery, B. E., and Singer, Charlotte: The Self-Disinfecting Power of the Skin as a Defense Against Microbic Invasion, Am. J. Hyg. **11**:345, 1930.

18. Talbert, G. A.: Effect of Work and Heat on the Hydrogen-Ion Concentration of the Sweat, Am. J. Physiol. **50**:433, 1919; Further Studies on the Hydrogen-Ion Concentration of Human Sweat, ibid. **61**:493, 1922.

than that from uncovered parts. Schade and Marchionini,[19] in interesting studies employing both the potentiometer and the indicator methods, found that the skin surface shows a p_H of 3.5. They expressed the belief that the acidity of the skin surface depends on the evaporation of sweat. Visible sweat diminishes the skin surface acidity, but on evaporation of the sweat, the acidity increases. Consequently, delayed evaporation, from whatever cause, interferes with the normal acid reaction of the skin surface. Evaporated sweat, through its acidity, seems to act like a protective covering for the skin against bacteria. Apocrine sweat has a higher p_H than eccrine sweat, and may occasionally be alkaline in reaction. This conclusion was also reached by Brill.[20] Both Brill and Marchionini reported that sweat obtained from the injection of pilocarpine is more alkaline than heat sweat. It is interesting to note in connection with the foregoing observations that various dermatoses appear in regions where apocrine sweat is present and in intertriginous places where sweat evaporation is delayed and the protective acid reaction is consequently lost.

Scholtz,[21] working with indicators, found that after washing the skin with soap, the p_H was increased to 6.0-6.3, and remained so for two hours. After four hours the reaction returned to the approximately normal figures of 5.7-5.8, and only after twenty hours were the figures again entirely normal. After the application of acids and their immediate removal with cotton soaked in benzine, the p_H remained at 5.2. In employing the indicator method, Scholtz found that in scaly dermatoses the p_H varied between 5.4 and 6.0; in papular eczemas, between 5.6 and 6.1, and in exudative eczemas, between 6.2 and 6.8, after removal of the secretion.

Lustig and Perutz[22] studied the reaction of the skin surface by spreading on the skin for a period of ten minutes flat layers of cotton previously soaked in distilled water, and then determining the p_H of the fluid in the cotton by the indicator method of Wulff. They found that

---

19. Schade, H., and Marchionini, A.: Der Sauremantel der Haut, Klin. Wchnschr. **7**:12, 1928; Zur physikalischen Chemie der Hautoberfläche, Arch. f. Dermat. u. Syph. **154**:690, 1928. Marchionini, A.: Physikalisch-Chemische Untersuchungen über ekkrinen und apokrinen Schweiss, Schweiz. med. Wchnschr. **58**:1055, 1928; Untersuchungen über die Wasserstoffionenkonzentration der Haut, Arch. f. Dermat. u. Syph. **158**:290, 1929.

20. Brill, E.: Ueber den Säuregehalt des menschlichen Schweisses bei Haut-Kranken und Hautgesunden, Arch. f. Dermat. u. Syph. **156**:488, 1928.

21. Scholtz, W.: Ueber Säure Behandlungen von Hautkrankheiten, Klin. Wchnschr. **9**:1670, 1930.

22. Lustig, B., and Perutz, A.: Ueber ein einfaches Verfahren zur Bestimmung der Wasserstoffionenkonzentration der normalen menschlichen Haut-Oberfläche, Arch. f. Dermat. u. Syph. **162**:129, 1930.

the acidity diminished after profuse sweating and after washing of the skin with soap solutions, but increased after cleansing the skin with benzine.

Employing the same method, Perutz and Lustig [23] determined the reaction of the skin surface in various dermatoses. They found that in a case of dermatitis of the fingers due to alkaline fluids, there was only a slight increase over the normal, the p_H of the injured parts being 5.5-5.9 as compared with a p_H of 5.3 of the control. In hyperhidrosis they found a slightly increased acidity. In acute eczema marked only by swelling and redness, there was a slight increase of acidity, the p_H being 5.0-5.6. The lower figures were obtained after washing the surface with benzine. In acute eczema accompanied by oozing their findings indicated a shift to the alkaline side, showing a p_H of 5.7-6.7. In seborrheic and chronic eczema they failed to discover any definite shift either to the alkaline or to the acid side.

PROBLEM AND PROCEDURE

Experiments were performed to determine the actual difference in the reaction of the skin surface in eczema as compared with that of the normal skin. In order that the skin surface when tested should be in the same condition as when first observed in practice, we avoided any special preparation of the skin surface, merely eliminating all exogenous substances such as salves, lotions or solutions that the patients might have applied. When topical preparations were used, no applications were made for twenty-four hours prior to the tests, and the surface was bathed with plain water to remove all foreign particles.

The quinhydrone electrode potentiometer was employed for determining the reactions of the skin surface. The construction of the gold and calomel electrodes was modified to facilitate contact with different parts of the surface without disturbing the apparatus.

The quinhydrone electrode potentiometer offers an easy, rapid and sufficiently accurate method of determining the p_H of the skin surface. In accuracy it compares favorably with the hydrogen electrode. When employed to determine the reaction of the skin surface, it is considered superior to the indicator method, since it enables one to take numerous readings in limited areas in a comparatively short time, and eliminates the color interpretation factor and the problem of "off-colors."

The quinhydrone electrode is made of gold or platinum. For this study the gold electrode was used. The electrode, when placed in a solution containing a small quantity of quinhydrone, acquires a potential definitely related to the hydrogen ion concentration of the solution. The p_H value is found from the measured voltage.

Quinhydrone is a compound in which quinone and hydroquinone are combined in equimolecular proportions. When it is dissolved, it dissociates into these two substances, one of which ionizes. In a solution containing hydrogen ions and dissociation products of quinhydrone, the potential of the electrode is directly related

23. Perutz, A., and Lustig, B.: Ueber die Wasserstoffionenkonzentration der Hautoberfläche und ihre Regulation bei Dermatosen, Arch. f. Dermat. u. Syph. **163**:18, 1931.

to the p_H value and the temperature of the solution. Quinhydrone is so slightly soluble in acid mediums that only a small quantity is necessary to saturate a sample for p_H measurement and to provide an excess that will insure the presence of its dissociated products. In solutions in which the alkalinity is over p_H 8,

TABLE 1.—*Cases and Reactions*

	Case	Sex	Age	Diagnosis	Normal Skin, p_H	Eruption, p_H
1.	C. K.	Female	24	Acute eczema	4.00	5.19
2.	G. C.	Female	10	Acute eczema	....	7.38
3.	T. L.	Male	58	Acute eczema	....	7.25
4.	J. R.	Male	53	Generalized eczema	....	6.76
4A	J. R.	Male	53	After several days' use of solution of aluminum acetate	....	6.10
5.	A. H.	Female	5	Chronic eczema	5.26	6.46
6.	H. L.	Male	27	Chronic eczema with areas of acute lesions	5.44	6.80
7.	H. S.	Male	68	Acute eczema and ulcer; chronic eczematous patches	5.40	7.60 5.80
8.	E. W.	Female	12	Acute eczema	6.67	8.00
9.	L. S.	Male	68	Acute eczema	6.60	7.20
10.	I. S.	Female	42	Chronic eczema	6.50	6.55
11.	R. L.	Male	35	Acute eczema	5.45	6.55
12.	B. E.	Male	69	Acute eczema	5.47	6.90
13.	J. R.	Male	40	Acute eczema	5.40	6.90
14.	T. K.	Male	66	Generalized eczema	....	6.50
15.	E. E.	Female	16	Acute eczema	....	6.97
16.	J. D.	Female	38	Acute eczema	5.75	6.80
17.	E. A.	Female	58	Chronic eczema	6.70	5.80
				With acute lesions	....	7.06
18.	T. R.	Male	53	Chronic eczema	5.20	5.70
				With acute lesions	....	6.20
19.	H. T.	Male	54	Acute eczema	5.30	6.00
20.	R. B.	Female	40	Chronic eczema	4.93	5.13
				Intertrigo with more moisture	....	6.20
21.	F. W.	Female	12	Acute eczema	6.00	7.20
22.	W. M.	Male	75	Acute eczema	5.82	6.50
23.	J. R.	Male	43	Erythroderma	....	6.70
24.	W. N.	Male	75	Acute eczema	....	6.39
25.	M. E.	Male	27	Seborrheic eczema	5.35	4.34
				After induced sweating	5.88	6.77
26.	E. L.	Male	55	Acute eczema	5.80	6.50
				After induced sweating	6.80	6.70
27.	B. E.	Male	69	Acute eczema	5.38	6.95
				After induced sweating	6.36	7.33
28.	S. L.	Male	55	Chronic eczema	5.70	5.41
				After induced sweating	....	5.48
29.	T. Q.	Male	48	Tabes	3.90	....
				After induced sweating	5.20	....
30.	T. K.	Male	35	Psoriasis	5.32	....
				After induced sweating	5.46	....

TABLE 2.—*Results of Experiment (Case 31)* *

	Minutes							
	0	5	10	15	20	30	40	50
Sweat from right leg	5.7	...	5.6	...	5.3	...	4.8	...
Sweat from arm	6.0	...	6.0	...	5.8	...	...	4.9
Sweat from left leg	...	5.4	...	...	...	4.9	...	...
Sweat from trunk	...	...	...	5.15	...	5.1	...	...

* Case 31.—A. L., a man, aged 36. This experiment was made to show the change, an increase, in the hydrogen ion concentration of sweat after standing and evaporation. Perspiration was induced in the radiant heat cabinet.

quinhydrone is more soluble and the hydroquinone dissociates and oxidizes; the proper ratio of quinone to hydroquinone is not maintained, and the potential of the electrodes is altered to such an extent that the measured voltage is no longer a linear function of the p_H. In the determination of the p_H of the skin surface, the reaction obtained is as a rule under p_H 8. In cases in which a higher reading is

obtained, it must be interpreted only as having a p_H above 8; it is impossible in such cases to determine with any accuracy the exact degree above 8.

The skin surface to be tested was sprinkled with a slight amount of quinhydrone from an atomizer. At times about 0.25 or 0.5 cc. of distilled water had to be added to provide sufficient fluid mediums for the determination.

In the first group of cases the reactions of both diseased and normal skins were examined. The sweat from patients who had perspired freely after being in the radiant heat cabinet was studied. For comparison with cases of eczema, the skin reactions of subjects with normal skin and of those with other dermatoses were tested. Also included were the results of tests performed on a patient with psoriasis who was under treatment. To learn whether perspiration changes its reaction on evaporation, we placed 2 cc. of sweat in three 50 cc. beakers and studied the hydrogen ion concentration at various intervals.

Owing to a lack of space, it is impossible to include the complete tables presenting the figures as found in the areas of eruption and in normal skin areas.

COMMENT

The tests performed on patients presenting various forms of eczema revealed an abnormal condition of the hydrogen ion concentration of the skin surface, and the disturbed reaction was invariably to the alkaline side. However, the degree of alkalinity varied. This was to be expected. The hydrogen ion concentration would be likely to depend on conditions productive of changes in the skin reaction, such as the stage of the eruption, the amount of vesiculation, oozing and crusting, the reaction of the cellular tissue and the multiform character of the skin itself. However, in chronic eczema, in which only such features as lichenification or scaling were present, the increase in the p_H was absent or very slight.

The greatest decrease in the hydrogen ion concentration was obtained in conditions similar to those in our cases 2, 3, 7, 8, 9 and 21. The oozing and crusting were pronounced in these cases, and in some there was a destruction of the superficial horny layer by the underlying vesicles. When some of the acute features of the eruption were absent, the increase in the p_H was not as marked. When both the acute and the chronic stages of the eruption were present, as in case 17, the acute patches showed a marked swing to the alkaline side, and the chronic patches, merely a slight deviation from the normal p_H. The p_H of the chronic scaly seborrheic infection of the scalp (in case 21) was lower than that obtained from the apparently normal skin surface of the chest. However, this patient showed an increased p_H of normal skin surface. Increased visible sweating, due to nervousness and fright, may have caused the change in the hydrogen ion concentration of the skin surface.

In case 4A a decrease in the p_H was observed, the reaction being less abnormal than that observed in case 4. For five days the patient had applied to his body an ointment of solution of potassium acetate having a p_H of 4.1. His general condition had also improved.

In all cases in which readings of the p_H of the axillae were compared with those of other portions of normal skin, we found an increased p_H. The decreased hydrogen ion concentration in the axillae is due both to the presence of apocrine sweat glands, which give forth a secretion of a higher p_H than that found in other places on the body, and to the fact that evaporation of the secretion is delayed because of the opposing skin surface.

The hydrogen ion concentration of the intact skin surface depends on two important factors: the intact horny layer and the evaporated secretion of the skin, interference with which will affect the reaction. The intact keratin layer of the superficial epidermis reacts acid, giving a p_H of about 5.0 to 5.5, as reported by many observers (Sharlit and Scheer, Memmesheimer, Perutz, Lustig, Scholtz, Lloyd and others), who cleared the skin of all secretion, then applied an indicator and observed the change in color. This test can easily be performed by cleaning the skin with benzine, applying a few drops of methyl red and observing the color change to orange.

Our conception of the skin surface should not be that of a horny layer alone, but should include the idea of a layer of evaporated chemicals resulting from the evaporation of the skin secretions, mainly sweat. This covering of evaporated chemicals is an important factor in maintaining the acid skin reaction, since perspiration on evaporation changes its p_H to the acid side. In experiment 31, we placed 2 cc. of freshly collected sweat in three beakers and tested the p_H at various intervals. We observed a decrease in the p_H after standing and evaporation.

That delay in evaporation has a tendency to increase the p_H was shown in case 20. This patient presented a scaly lichenified eruption which showed little deviation from the normal reaction. The p_H of the same lesion under the breast, where slight maceration and moisture were present, was distinctly more alkaline. The tests of chronic seborrheic dermatitis did not reveal an increased p_H.

Case 28 was of particular interest. The patient for some reason very seldom washed his skin, and inspection revealed that he had not taken a bath for several months. The reaction of the skin surface was, however, within normal limits. This case points out clearly the peculiar ability of the skin surface to retain its normal reaction.

We included for the sake of comparison a case that did not present any skin lesion, and tests of the normal skin surface in a case of psoriasis in which the patient was under treatment. The reaction of the skin surface in the former (a case of tabes dorsalis) showed a p_H lower than that usually encountered in most normal skin cases.

Visible perspiration has a definite effect on the reaction of the skin surface, tending in certain cases to make the reaction more alkaline. In the case of seborrheic eczema, the reaction of the skin surface became

more alkaline after sweating because the sweat was more alkaline than normal. The ability of the skin surface in our case 28 to give a distinctly acid p_H was most likely due to the fact that the reaction of the perspiration was definitely acid, so that the evaporation of sweat maintained the skin surface reaction.

CONCLUSIONS

1. The quinhydrone electrode potentiometer offers an easy, rapid and accurate method for the determination of the reaction of the skin surface.

2. The skin surface reaction in health is acid, having a p_H of from about 5 to 5.3.

3. The hydrogen ion concentration of the skin surface depends on (*a*) the intact keratin layer and (*b*) the evaporated chemicals of the skin secretions, mainly sweat.

4. When the continuity of the horny layer is disturbed or the evaporation of sweat is delayed, the reaction of the skin surface is changed.

5. The intertriginous areas show a lowered H-ion concentration.

6. Visible perspiration tends to raise the p_H of the skin surface.

7. Sweat on standing and evaporation increases in acidity.

8. The p_H in the axillae is higher than on the skin of the chest.

9. The lowered acidity of the axillae is due to the apocrine sweat secreted and to delayed evaporation.

10. The fact that one of our patients did not bathe for many months did not alter the reaction of the skin surface.

11. In acute and subacute eczematous conditions, the hydrogen ion concentration of the skin surface is lowered. The p_H is slightly above or below the neutral point.

12. In chronic eczematous eruptions in which lichenification and scaling of the skin are prominent, the reaction is very slightly altered.

13. The reaction of the skin surface in erythroderma was markedly to the alkaline side.

14. A tendency to return to the normal skin reaction was noted in one case of erythroderma, on improvement after the application of a salve, the p_H of which was 4.1.

15. Finally, it is intended to show, as a result of these experiments, in a subsequent report, the rationale for the topical applications in eczema.

2 East Fifty-Fourth Street.

INFLUENCE OF VIOSTEROL HYPERCALCEMIA ON SKIN IRRITABILITY OF DOGS

ARTHUR G. SCHOCH, M.D.
DALLAS, TEXAS

Wright [1] was probably the first to use calcium therapy in dermatology thirty-five years ago in the treatment for urticaria. Since then calcium therapy has been widely used in the treatment for urticaria, eczema and dermatitis. There seems to be fairly general agreement that calcium therapy is of distinct value in the treatment for certain dermatoses. Nearly all of the favorable results reported are based on clinical evidence. Attempts to demonstrate the mode of action of calcium in animals, as well as attempts to show calcium deficiencies in patients with urticaria and dermatitis, have, for the most part, been unsuccessful. The futility of seeking a relation between minor fluctuations of serum calcium values and inflammations of the skin in patients has been demonstrated by Klauder and Brown,[2] Schamberg and Brown,[3] Brown and Greenbaum,[4] Nathan and Stern [5] and others.

Submitted for publication, June 26, 1931.

From the Department of Physiological Chemistry and the Department of Dermatology and Syphilology, School of Medicine, University of Pennsylvania.

1. Wright, A. E.: Notes on Two Cases of Urticaria Treated by the Administration of Calcium Chloride, Brit. J. Dermat. **8**:82, 1896.

2. Klauder, J. V., and Brown, Herman: Experimental Studies in Eczema: I. Study of the Sensitivity of the Skin of Rabbits to Chemical Irritants under Experimentally Induced Conditions, Arch. Dermat. & Syph. **11**:283 (March) 1925; II. A Correlation of the Chemistry with the Irritability of the Skin of Animals under Normal and under Experimentally Induced Conditions, ibid. **15**:1 (Jan.) 1927; III. The Rate of the Sympathetic Nervous System and Calcium-Potassium Ratio in Altering Cutaneous Irritability in the Rabbit, ibid. **19**:52 (Jan.) 1929; IV. A Correlation of Potassium-Calcium Ratio in the Serum and in the Skin of Rabbits with the Irritability of the Skin, ibid. **20**:326 (Sept.) 1929; V. Studies of the Potassium, Total and Diffusible Calcium Ratios in Blood of Patients with Diseases of the Skin, ibid. **22**:877 (Nov.) 1930.

3. Schamberg, J. F., and Brown, Herman: A Study of Inorganic Salts in the Blood in Psoriasis and Certain Other Dermatoses, Arch. Dermat. & Syph. **9**:368 (March) 1924.

4. Brown, Herman; and Greenbaum, S. S.: Blood Calcium Distribution in Urticaria, Brit. J. Dermat. **42**:183 (April) 1930.

5. Nathan, E., and Stern, F.: Ueber Kalium und Calciumschwankungen im Blutserum bie Dermatosen; Arch. f. Dermat. u. Syph. **156**:446, 1928.

In the studies of Luithlen,[6] of Klauder and Brown,[2] of Januschke[7] and of Cantarow and Gordon,[8] attempts have been made to alter experimentally the mineral metabolism and to observe the response of the skin to irritants. Luithlen used various diets to alter the mineral metabolism in rabbits. Januschke found that administration of calcium salts in large doses and narcosis diminished the effect of volatile oil of mustard U. S. P., instilled into a rabbit's eye. Klauder and Brown, in an extensive study of the mineral metabolism in rabbits and its relation to the skin irritability, used both regulation of diet and injection of drugs as methods of altering the mineral metabolism of the animals. They concluded that skin irritability could not be correlated with serum calcium, but that it did bear a direct relation to the potassium-calcium ratio of the blood serum and of the skin itself. Later, in studying patients with different dermatoses, they could not correlate the potassium-calcium ratio with skin irritability.

Cantarow and Gordon, in studying patients, used parathyroid extract to alter the calcium metabolism. The blister time (the time required for vesiculation to take place after the removal of a cantharides plaster) was used as the method of treatment for skin irritability. They concluded that the increased available circulating calcium seemed to have a slight but definite inhibitory effect on inflammatory edema. This inhibitory effect was noted in two thirds of the patients studied. Changes in serum calcium values were slight at the most.

Jones, Rapaport and Hodes[9] were able to produce pronounced hypercalcemia in dogs by daily administration of viosterol by mouth. As hypercalcemia may be produced readily by this means, it was thought worth while to study the skin irritability after producing the condition. Irritability was tested by means of various dilutions of croton oil in olive oil.

Klauder and Brown[2] have pointed out that in rabbits pigmented skin reacted with much less intensity than nonpigmented skin. In this study, the same observation was made on the skin of dogs.

---

6. Luithlen, F.: Tierversuch über Hautreaction, Wien. klin. Wchnschr. **24**: 703, 1911.

7. Januschke, H.: Ueber Entzündungshemmund, Wien. klin. Wchnschr. **26**: 869, 1913.

8. Cantarow, A., and Gordon, B.: The Effect of Parathyroid Extract on Certain Factors Underlying the Production of Edema, Arch. Int. Med. **42**:939 (Dec.) 1928.

9. Jones, J. H.; Rapaport, M., and Hodes, H. L.: The Source of Excess Calcium in Hypercalcemia Induced by Irradiated Ergosterol, J. Biol. Chem. **89**:647 (Dec.) 1930.

METHOD

Dogs with nonpigmented skins were selected. The dogs were allowed two weeks in which to adjust themselves to the cages in the animal house and to the diet of hospital scraps. Samples of blood were taken by heart puncture, and serum calcium values were determined by Clark and Collip's [10] modification of Tisdall's method.

Normal skin responses to various dilutions of croton oil in olive oil were then determined. For this purpose, six different dilutions of croton oil were used, 1:5, 1:10, 1:20, 1:40, 1:60 and 1:80. The hair was clipped (not shaved) as closely as possible over the back and sides of the chest without injuring the skin. The test solutions of croton oil were applied by means of small linen patches (2 cm.

Readings Indicating Severity of Skin Reactions *

Dilutions of Croton Oil	1				2				3				4				Comment
	a	*b*	*c*	*d*	*a*	*b*	*c*	*d*	*a*	*b*	*c*	*d*	*a*	*b*	*c*	*d*	
Dog 1 (control)																	
1:5	4	4	4	4	4	4	4	4	4	4	4	4	3	3	3	3	Control animal kept on same diet and under same conditions as other animals. Bled same number of times as other animals
1:10	3	3	3	2	3	3	3	2	3	3	3	1	3	3	3	2	
1:20	3	3	2	2	3	3	2	0	3	2	2	0	3	3	2	0	
1:40	2	2	1	1	2	2	1	0	2	2	1	0	2	2	1	0	
1:60	1	1	1	0	1	1	1	0	1	1	1	0	1	1	1	0	
1:80	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	Calcium 11.8				12.0				11.9				11.7				
Dog 2 (Viosterol Hypercalcemia)																	
1:5	4	4	4	4	4	4	4	4	4	4	4	4	3	3	3	3	Viosterol (1,500 D) 0.15 cc. per kilogram of body weight given by mouth daily for three weeks, then readings in column 3 were made
1:10	3	3	2	0	3	3	3	3	3	3	3	3	3	3	3	3	
1:20	3	2	1	0	3	3	2	2	3	2	2	2	3	3	3	2	
1:40	2	2	1	0	2	1	1	0	2	1	1	0	3	2	1	0	
1:60	2	2	0	0	2	1	1	0	1	1	1	0	2	2	1	0	
1:80	1	0	0	0	1	0	0	0	1	0	0	0	1	1	0	0	
	Calcium 11.7				11.5				19.8				11.9				
Dog 3 (Viosterol Hypercalcemia)																	
1:5	4	4	4	4	4	4	4	4	4	4	3	3	4	3	3	3	Viosterol (1,500 D) 0.15 cc. per kilogram of body weight given by mouth daily for three weeks, then readings in column 3 were made
1:10	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	
1:20	3	3	3	3	3	3	3	2	3	3	2	2	3	3	3	2	
1:40	2	2	1	0	3	2	2	2	2	2	1	0	2	2	2	1	
1:60	1	1	0	0	1	1	1	0	1	1	0	0	1	1	0	0	
1:80	1	0	0	0	1	1	0	0	1	1	0	0	1	0	0	0	
	Calcium 11.1				11.0				18.2				12.1				
Dog 4 (Thyroidectomy)																	
1:5	3	3	3	3	3	3	3	3	3	2	2	2	.....				Thyroidectomy (parathyroids intact). After three weeks readings in column 3 were made
1:10	3	3	3	3	3	3	3	3	3	2	2	2					
1:20	3	3	3	3	3	3	3	3	2	1	0	0					
1:40	3	2	2	2	3	3	2	2	2	0	0	0					
1:60	3	2	2	1	3	3	2	2	0	0	0	0					
1:80	2	1	1	0	2	1	1	0	0	0	0	0					
	Calcium 10.8				10.5				10.4				10.0				

* Dilutions of croton oil in olive oil used as test solutions designated in extreme left column; 1:20 means one part croton oil and twenty parts olive oil. Column 1 represents block readings over a period of one week; column *a* read vertically gives readings obtained immediately after removal of test solutions; columns *b*, *c* and *d* represent readings at the end of twenty-four hours, forty-eight hours and one week, respectively. Columns 1 and 2 are normal readings three weeks apart. Column 3 includes readings taken three weeks after experimental procedure was instituted. Column 4 includes readings made two months later. Average serum calcium concentrations in mg. per hundred cubic centimeters are given at the bottom of each block of readings.

10. Clark, E. P., and Collip, J. B.: A Modification of the Serum Calcium Method of Tisdall, J. Biol. Chem. **63**:461, 1925.

square) saturated with the solution. They were covered with squares of tracing cloth about twice the size of the linen patches, and these were then bound tightly to the skin with adhesive plaster. Two inch (5 cm.) gauze bandages were applied on top of the adhesive plaster to insure good contact of the test solution with the skin, and finally, heavy cloth jackets were tied onto the animals to prevent them from removing the test solutions.

At the end of twenty-four hours, the test solutions were removed and the readings were made (column 1*a*). A discernible reaction in the form of erythema was designated as 1, erythema with a few scattered papules as 2, added edema and vesiculation as 3, and when frank necrosis was present, the reaction was designated as 4.

After another twenty-four hours the test sites were read again in the same manner (column 1*b*). The third reading was taken forty-eight hours after removal of the test solutions, and the fourth reading (column 1*d*) was made one week after application of the irritant. In this manner any great change in the rapidity of involution of the test sites could be detected.

At the end of two weeks, a second normal block reading was made in the same manner. In this way two sets of normal readings were made on each animal (columns 1 and 2).

Dog 1 was kept as a control. Skin instability tests were done on this animal every time they were done on dogs 2, 3 and 4.

Dogs 2 and 3 were given 0.15 cc. of viosterol (1,500 D) per kilogram of body weight by mouth, daily for three weeks. Serum calcium determinations were made at five day intervals, and when the serum calcium concentrations reached 18 mg. per hundred cubic centimeters or above, the skin irritability was again determined (column 3). The viosterol feeding was then stopped, and the dogs were allowed two months in which to recover from the effect. One month is usually sufficient to permit the serum calcium to return to a normal level. The skin irritability was then again tested. These results are seen in column 4.

RESULTS

From the table it will be seen that there was no appreciable change in the skin irritability of dogs 2 and 3 during the stage of extreme hypercalcemia due to ingestion of viosterol.

There seemed to be a slight diminution in the skin irritability of dogs 2 and 3 in the last reading after the blood serum calcium had returned to normal (column 4). It will be noticed that this same slight diminution occurred with dog 1, which was the control animal. Sandek showed that the skin of rabbits acquired an immunity against the cutaneous irritant, volatile oil of mustard. Although care was taken not to place the test solutions on previous test sites, it is possible that by the time the fourth block test was applied, the skin as a whole had acquired some degree of immunity to the irritant.

The effect of thyroidectomy was studied on one dog. The thyroid glands were removed from dog 4, special care being taken to preserve four parathyroid glands. Fifteen days after operation, the skin irritability was retested (column 3), and found to be definitely reduced. The parathyroid glands in this animal were functioning sufficiently to

maintain the normal serum calcium concentrations. Definite conclusions cannot be drawn from results obtained in one animal. The reduction of skin irritability, however, in this dog was striking. Any study of the skin irritability of thyroparathyroidectomized dogs, associated with hypocalcemia, would have to take into account the possible effect of thyroidectomy on skin irritability.

SUMMARY

1. No perceptible change in the skin irritability of dogs was demonstrated as a result of hypercalcemia caused by the administration of viosterol.[11]

2. All the animals, including the control, showed a slight diminution of skin irritability at the end of the experiments. This slight reduction was interpreted as an acquired tolerance or immunity to the cutaneous irritant resulting from previous applications.

3. In one animal (dog 4), skin irritability was reduced following thyroidectomy.

11. Mead Johnson & Company supplied the irradiated viosterol used in this study.

LOCAL RESPONSES TO HISTAMINE IN NORMAL SKIN, IN DERMATOPHYTOSIS, IN ALOPECIA AREATA AND IN SCLERODERMA

ALLEN D. KING, M.D.
PHILADELPHIA

There are features of certain dermatoses which indicate that local alterations of cutaneous circulation may be concerned in their etiology. This paper contains the investigative study of the cutaneous circulation in three of these conditions, namely, epidermophytosis of the feet, alopecia areata and scleroderma. The work is based on the urticarial reaction of the skin to histamine applied intradermally, and the results are compared with those obtained from one hundred normal control cases.

The histamine wheal was first reported by Eppinger [1] in 1913. It was studied further by Sollmann and Pilcher [2] in 1917. Dale and Richards [3] made an extensive investigation of the pharmacologic action of histamine, and concluded that it caused dilatation of the capillaries by decreasing the tone of these vessels. Lewis [4] very ingeniously has shown that the normal skin gives a constant reaction to histamine, characterized by the formation of a central wheal and surrounding flare. He and his collaborators [5] have proved this reaction to be of a threefold character, terming it the "triple response." First, there is formed a small red spot due to local capillary dilatation. This is followed quickly by a reflex arteriolar dilatation (flare), and is attended in from two to four minutes by the formation of a wheal at the site of the original red spot. The wheal depends on the blood flow, being delayed or inhibited as the arterial circulation is impaired; the flare is a function of the local nerve reflex and is absent after degeneration of the peripheral nerve.

Submitted for publication, July 6, 1931.

From the Department of Dermatology and Syphilology, School of Medicine, University of Pennsylvania, and the Dermatological Clinic of the University Hospital, Dr. John H. Stokes, Director.

1. Eppinger, H.: Wien. med. Wchnschr. **23**:1414, 1913.

2. Sollmann and Pilcher: J. Pharmacol. & Exper. Therap. **9**:309 (March) 1917.

3. Dale and Richards: J. Physiol. **52**:110 (July) 1918.

4. Lewis, T.: Blood Vessels of Human Skin and Their Responses, London, Shaw & Sons, Ltd., 1927.

5. Harris, K. E.: Heart **14**:161 (Dec.) 1927. Jones, T. D.: ibid. **14**:339 (March) 1929.

Starr [6] applied this histamine reaction to a study of the circulation in the feet of patients with diabetic arteriosclerosis, and found it impaired or absent in cases of threatened or actual gangrene. Furthermore, by testing at various levels of the limb, he demonstrated that a fairly accurate estimate of the level for amputation could be obtained. Caldwell and Mayo [7] studied vascular occlusive diseases by means of the histamine reaction, and found the reaction to be delayed and reduced in the affected limbs.

Rondelli [8] investigated the response of the skin to histamine in a series of cases composed largely of hypertension, nephritis and cardiac disease. He came to the conclusion that the test was of value in portraying the state of the minute vessels of the skin in pathologic conditions of the circulation. His technic differed from Starr's in that he made but one application of histamine intradermally through a

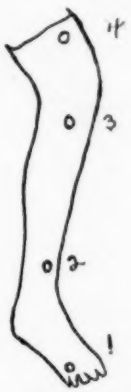

Fig. 1.—Experimental test sites.

hypodermic needle, and readings were taken at intervals of five minutes, thirty minutes and one hour.

Roxburgh [9] studied the circulation in areas of alopecia areata by the histamine picture. His conclusions will be referred to later.

METHOD

A 1:1,000 aqueous solution of histamine acid phosphate was used. The technic, that of Starr, consisted of the application of 1 drop of the solution to the skin, pricked in with seven pricks of a needle. The tests were made at four places on each leg as follows: (1) the dorsum of the foot at the base of the little toe, (2)

6. Starr, I., Jr.: Change in the Reaction of the Skin to Histamine, J. A. M. A. **90**:2092 (June 30) 1928; Am. J. M. Sc. **180**:149 (Aug.) 1930.

7. Caldwell, J. M., and Mayo, J. G.: Cutaneous Reactions to Histamine, Arch. Int. Med. **47**:403 (March) 1931.

8. Rondelli, U.: Minerva med. **8**:850 (Dec. 8) 1928.

9. Roxburgh, A. C.: Brit. J. Dermat. **41**:351 (Oct.) 1929.

above the external malleolus of the fibula, (3) just below the head of the fibula and (4) over the internal condyle of the femur. Readings were made at intervals of two and one-half, five, seven and one-half and ten minutes after the skin puncture. The results were recorded by means of sketches. During the tests the temperature and the position of the limbs must be kept constant. As clear daylight is essential to a correct reading of the flare, no tests were made on murky days or by artificial light.

RESULTS

The Reaction in Cutaneously Normal Persons.—One hundred white medical and surgical patients in the wards of the University Hospital were used. These cases showed no evidence of any dermatoses or of vascular disease.

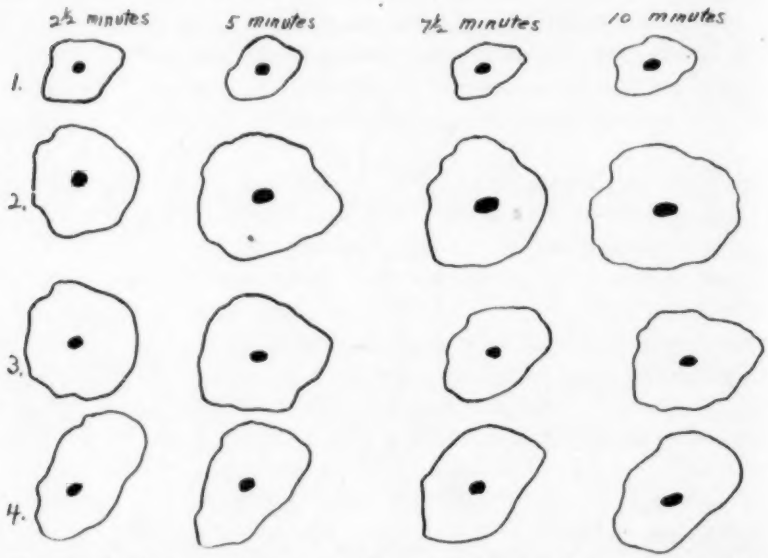

Fig. 2.—Typical reaction: *1*, reaction on foot at various time intervals; *2* wheal and flare above ankle; *3*, whealing flare below the knee; *4*, whealing flare above the knee.

A wheal that appears within two and one-half minutes of skin puncture and that is accompanied by a flare approximately 2.5 cm. in diameter should be considered a normal reaction. A typical response is shown in figure 2.

Moderate variations occurred, chiefly in the size and visibility of the flare. Ten per cent of the patients showed some delay in "whealing." Eleven per cent had a difference in reaction between the two legs.

Early in the series it was apparent that the time of appearance of the wheal was far more constant and reliable than the size, intensity or rate of development of the flare. At times the irregular boundaries of the flare were difficult to determine, and might be obscured in deep

brunettes or in those with tanned skins. Whealing above the knee was prompt and full in every one of the one hundred normal persons. As a rule, the flare was also full-sized and distinct. This regularity of response was not encountered at sites below the knee.

The Reaction in Epidermophytosis.—Thirty-five patients were tested. All grades of activity of the infection were included.

Here again the results varied slightly, in much the same percentages as those encountered among the cutaneously normal persons. Eleven per cent showed a delay in whealing. Another fourteen per cent showed a difference in reaction between the two legs. There were no correlations between the variations of the reaction and the activity of the dermatophytic process (fig. 3). Instead, the results were in keeping with the minor venous anatomic differences in the circulation of the two legs.

TABLE 1.—*Results in One Hundred Cutaneously Normal Persons*

Normal Reactions	Delayed Whealing	Small Flares	Faint Flares	Variations Between Legs
54%	10%	25%	11%	11%

TABLE 2.—*Results in Thirty-Five Cases of Epidermophytosis*

Normal Reactions	Delayed Whealing	Small Flares	Faint Flares	Variations Between Legs
54%	11%	29%	11%	14%

The Reaction in Alopecia Areata.—Five cases of alopecia areata and of alopecia totalis were studied. In all of them whealing was prompt and normal. Flare responses varied, being of average size but having exceedingly irregular boundaries. There were no controls for comparison, but the results indicate that no severe vascular derangements, detectable by histamine test, were present in the hairless areas. These findings substantiate those of Roxburgh, who concluded that the response to histamine was essentially the same in denuded areas as in his control sites.

The Reaction in Two Cases of Scleroderma.—The reaction in the two cases tested differed clinically, one being an extensive morpheaform process and the other a localized process confined to the right leg. The extensive case showed an essentially normal reaction although the flare was undersized and slightly irregular. In the localized type, whealing was delayed along the affected limb and normal in the healthy limb. Flares were of good quality and size in both limbs.

Pigmentation as a Factor.—The size of the flare in blonds and brunettes was tabulated. It tended to be larger in blond subjects, probably because of the greater transparency of the epidermis. Of the patients with flares larger than 2.5 cm. in diameter, seven were blonds and six were brunettes. Of those with flares of 2.5 cm. diameter or less, brunettes outnumbered blonds more than two to one.

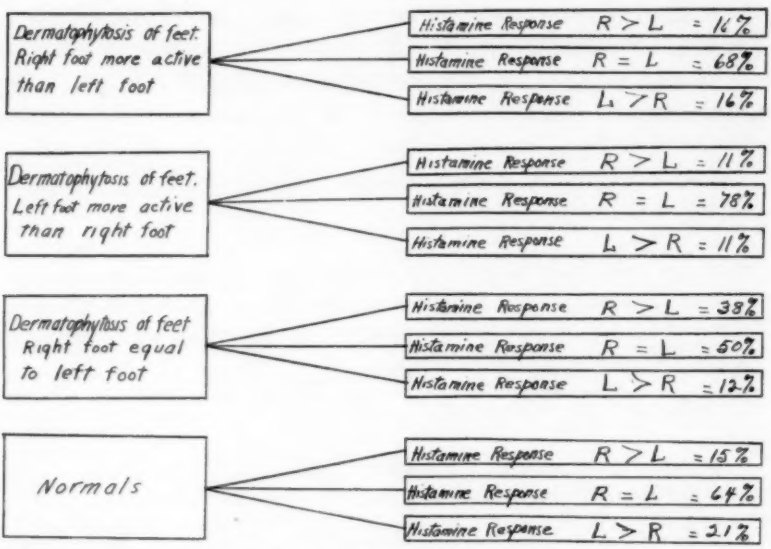
Dermatophytosis of feet. Right foot more active than left foot
Histamine Response R > L = 16%
Histamine Response R = L = 68%
Histamine Response L > R = 16%
Dermatophytosis of feet. Left foot more active than right foot
Histamine Response R > L = 11%
Histamine Response R = L = 78%
Histamine Response L > R = 11%
Dermatophytosis of feet Right foot equal to left foot
Histamine Response R > L = 38%
Histamine Response R = L = 50%
Histamine Response L > R = 12%
Normals
Histamine Response R > L = 15%
Histamine Response R = L = 64%
Histamine Response L > R = 21%

Fig. 3.—The response to histamine as compared to the activity of the dermatophytic process.

TABLE 3.—*Size of the Flare in Normal Persons: Blond Versus Brunette*

	Larger Than 2.5 Cm.	2.5 Cm.	Less Than 2.5 Cm.
Blond	7	6	9
Brunette	6	21	20

The tendency of fair blond skins to overreact to irritation is well known. In addition, the pigmentation of the brunette masks the outlines of the flare, causing the area to appear smaller.

SUMMARY

A study of the reaction of the normal skin to histamine piqûre, and that of the skin in dermatophytosis of the foot, in scleroderma and in the denuded areas of alopecia areata permits of the following comment and résumé.

The reaction to histamine piqûre applied to the lower extremities is normally more intense above the knee than below. It is conceivable that this relative irresponsiveness of the more dependent fields has protective utility in dealing with the greater hydrostatic pressure in the foot as compared with the upper part of the leg. There is distinctly a normal type of reaction in normal persons to which the observer can refer deviations. The size of the flare is of less importance than the time of appearance of the wheal. In fact, the flare is, in my opinion, a variable and untrustworthy element, unless it is possible to devise methods of mensuration of size, intensity and vascular behavior of the capillaries not as yet applied in these studies. Pigmentation is, moreover, a complicating element in the interpretation of the flare. The comparison of blonds and brunettes indicates that even a slight difference in pigmentation in the white race reduces the visibility and apparent area of the flare, and consequently its worth in the test. A method of measuring pigmentation will therefore be a necessary adjunct in comparative studies of flares. The flare is, of course, not usable in the colored patient. In normal persons there is a slight proportion of difference between the two legs in the matter of flare (11 per cent) variation and in the time of whealing. In this study, the reaction in the normal left leg was greater than that in the normal right leg in 21 per cent, and greater in the normal right leg than in the left in 15 per cent. This difference of 6 per cent may, of course, be part of the margin of experimental error, but, in any event, it is at the moment not precisely interpretable. It is worth further study as possibly associated with the anatomic circulatory differences in the venous supply of the two legs. This question will be raised again in connection with the response in dermatophytosis.

In dermatophytosis of the foot (clinically so diagnosed) interesting deviations from this possibly normal picture appeared. When dermatophytosis was more pronounced on one foot than the other, whether that foot was right or left, the suggested (normal?) difference in histamine response between the two feet was absent. On the other hand, when the two feet were equally involved, which should perhaps call for some change in vascular behavior of the right foot to make it the equal of the left in susceptibility, the right showed a more marked reactivity to histamine in 38 per cent, as compared with a more marked reactivity of the left in only 12 per cent. This difference of 26 per cent, while not offered as more than suggestive, may bear further investigation in studying the vascular background of fungus growth on the skin, especially of the extremities.

In five cases of alopecia areata, no abnormalities in histamine response were detectable in the involved areas. These findings sub-

stantiate those of Roxburgh and add weight against a vascular factor in the etiology of this condition.

The two cases of scleroderma examined showed conflicting results, possibly associated with differences in clinical type. The patient showing normal responses (allowing for pigmentation of certain areas) was on the road to recovery from a scleroderma that more resembled the confluence of multiple lesions of morphea than the masked face and blue, rigid, hide-bound and thickened hands of the more distinctly "sympathetic" type of scleroderma. The second patient with scleroderma tested had a diffuse involvement of the right leg, with accentuation in a linear band. In this case whealing was delayed, even above the knee, which agrees with the findings of Caldwell and Mayo in three cases.

TRICHOPHYTIN IN DIAGNOSIS

CHARLES M. WILLIAMS, M.D.
AND
CEDRIC C. CARPENTER, M.D.
NEW YORK

The active principle of the pathogenic fungi in the skin was first isolated by Scholtz [1] in 1918. Until recently the use of this extract has been limited to those who had the necessary facilities for its preparation, but since 1929, it has been obtainable from commercial laboratories. The purpose of this paper is to study, by means of the intradermal skin test, the accuracy of the product in the diagnosis of dermatomycoses of the glabrous skin.

False positive reactions of the skin are obtained in a high percentage of patients tested with extract contaminated by bacteria. Doctors Goodman and Litterer first demonstrated such results in the pathological laboratory of the Stuyvesant Square Hospital, and the fact has been fully confirmed in this series of cases. In most pseudopositive reactions, the skin responds with a marked local reaction, consisting of a large erythematous area surrounded by an exaggerated areola, which, in more susceptible persons, progresses to the formation of local abscesses.

Contamination may be prevented by the addition of 0.25 per cent phenol, according to Darier.[2] It was decided not to use this drug, as it was feared that it might produce a false positive reaction in some cases. Instead, a daily check on the sterility of the solutions was maintained by cultures, and only tests in which the extract was proved free from bacteria are reported.

TECHNIC

Trichophyton extract containing T. gypsum 40 per cent, T. cerebriforme 20 per cent, T. microides 20 per cent, T. rosaceum, T. violaceum and T. crateriforme, of each equal parts to 20 per cent, was used in sterile distilled water in dilutions of 1:20 and 1:50. A wheal was produced on the volar surface of the forearm by the injection of 0.1 cc. of this solution through a tuberculin syringe and a 26 gage ½ inch needle. Control injections were not made, as no broth is furnished

Submitted for publication, June 5, 1931.

From the Pathological Laboratory of the Stuyvesant Square Hospital, formerly the New York Skin and Cancer Hospital.

1. Scholtz, W.: Ueber die diagnostische und therapeutische Anwendung des Trichophytin Hochst, München. med. Wchnschr. **65**:509, 1918.

2. Darier, J.: Précis de dermatologie, Paris, Masson & Cie, 1928, p. 732.

by the laboratories for this purpose and because of the nature of the diluent. Therefore, the possibility of foreign protein sensitivity cannot be ruled out. Injections were made and the tests read by one of us (Dr. Carpenter). The extract used was from the same manufacturer's "lot," and the potency was probably constant.

INTERPRETATION OF TEST

In these concentrations, a satisfactory reaction varying between 1 and 3.5 cm. in diameter is obtained in forty-eight hours—the time at which all of our tests were read. The reaction usually takes the form of a simple erythema, but in some cases it is finely papular or papulovesicular, with an accompanying areola that is usually not broader than from 0.5 to 1.5 cm. A "depot" reaction of less than 1 cm. surrounding the site of the needle puncture cannot be considered of diagnostic signifi-

TABLE 1.—*Clinical Cases of Tinea with Positive Trichophytin Test*

	Character of Infection			
	Severe	Moderate	Mild	Total Cases
Laboratory positive	6	10	20	36
Laboratory negative	4	9	2	15
Total	10	19	22	51

TABLE 2.—*Clinical Cases of Tinea with Negative Trichophytin Test*

	Character of Infection			
	Severe	Moderate	Mild	Total Cases
Laboratory positive	1	1	3	5
Laboratory negative	3	7	4	14
Total	4	8	7	19

cance, and if the area is more than 4 cm. with a marked areola, contamination is to be suspected. The reaction of the 1:50 dilution was usually less in extent than that of the 1:20, but for the most part this difference is not important. In the whole series there were only two delayed reactions, one occurring at the end of five days and the other in ten days. These cases were not included in this series, as no reasonable explanation could be given for the phenomena.

RESULTS

In 73 per cent of the seventy cases reported in tables 1 and 2, the trichophytin reaction was positive, whereas, according to the microscopic and cultural methods, only 58.5 per cent were positive. The extract was positive in 88 per cent of the laboratory-proved cases. There was only one unaccountable positive reaction in the control group (table 3), or in 2.4 per cent of the total cases reported. This occur-

rence calls for an explanation, and two hypotheses suggest themselves: (1) that there was a persistence of sensitivity after all the symptoms at the site of the original focus had disappeared, or (2) that lesions not yet recognized as being dermatomycotic in origin had been overlooked.

TABLE 3.—*Control Group*

Analysis of Cases Studied	
Pityriasis rosea	22
Acne	9
Tinea versicolor	5
Miscellaneous dermatoses	5
Total	41
Cases with Negative Trychophytin Test	
Feet clinically and laboratory negative	14
Feet not examined	19
Mosaics in microscopic observations	2
Total	35
Cases with Positive Trichophytin Test	
Feet clinically positive and laboratory negative	2
Feet clinically positive and with microscopic mosaics	3
Unaccountable positive trichophytin test	1
Total	6

TABLE 4.—*Trichophytin Test in Patients with Pityriasis Rosea*

Trichophytin test negative	
Feet clinically and laboratory negative	6
Feet not examined	13
Feet clinically and laboratory positive	2
Trichophytin test positive	
Feet clinically and laboratory positive	5
Feet clinically positive	2
Feet clinically positive and with microscopic mosaics	1
Total cases reported	29

The occurrence of a positive reaction in cases in which only mosaics could be demonstrated is in accord with similar observations made by MacKee and Lewis,[3] using the patch test.

It has been generally believed that only deep infections give positive results with the trichophytin test. Von Graffenried[4] and Peck,[5]

3. MacKee, G. M., and Lewis, G. M.: Keratolysis Exfoliativa and the Mosaic Fungus, Arch. Dermat. & Syph. **23**:445 (March) 1931.

4. von Graffenried, C. R.: Dermat. Wchnschr. **6**:361 (May 25) 1918.

5. Peck, S. M.: Epidermophytosis of the Feet and Epidermophytids of the Hands, Arch. Dermat. & Syph. **22**:43 (July) 1930. (Reported on chart.)

however, have shown that positive tests may be obtained in cases in which the involvement is only superficial. Our series bears out the latter belief, as positive reactions were obtained in 87 per cent of the laboratory-proved cases of infections that were limited to the epidermal layers, which included the cases of three patients in whom the mycelia could be recovered only from the nails.

Generalized manifestations of an allergic nature following the intradermal use of trichophytin extract have been recorded. As Sulzberger and Kerr,[6] Wise and Sulzberger,[7] Ramirez[8] and Peck[9] have shown, these manifestations may take the form of urticaria, asthma, hay fever, febrile states and an aggravation of existing trichophytids. None of these complications were met with in our use of the test, nor were any unpleasant local reactions encountered.

There has been some recent discussion as to whether the secondary generalized eruption of pityriasis rosea may not be a trichophytid. Goodman[10] again raised this question because of a series of positive tricophytin tests which he obtained in this disease; however, he had similar results with acne. Van Dyck[11] reported similar results in his cases of pityriasis rosea. Of the twenty-nine cases of this disease that we studied (table 4), positive reactions were obtained only in those that showed clinical or laboratory evidence of tinea infection of the feet.

SUMMARY

1. Seventy cases in which clinical diagnosis of tinea of the glabrous skin had been made were studied by laboratory means, and tests were made with extract of trichophytin injected intradermally.

2. Forty-eight patients with unrelated dermatoses were similarly studied as controls. Twenty-nine of them had pityriasis rosea.

---

6. Sulzberger, M. B., and Kerr, P. S.: Hypersensitiveness of Urticarial Type with Circulating Antibodies and Passive Transference, J. Allergy **2**:11 (Nov.) 1930.

7. Wise, F., and Sulzberger, M. B.: Urticaria and Hay Fever Due to Trichophytin, J. A. M. A. **95**:1504 (Nov. 14) 1930.

8. Ramirez, M. A.: Sensitization Case, M. J. & Rec. **132**:382 (Oct. 15) 1930.

9. Peck (footnote 5, p. 74).

10. Goodman, H.: Tinea: The Second Most Prevalent Disease of the Skin, Arch. Dermat. & Syph. **23**:873 (May) 1931.

11. Van Dyck, L. S.; Kingsbury, J.; Throne, B., and Myers, C. N.: Use of Trichophytin as a Diagnostic and Therapeutic Agent in Mycotic Infections of the Skin, New York State J. Med. **31**:611, 1931.

CONCLUSIONS

1. False positive trichophytin tests may be obtained if the extract is contaminated with bacteria.

2. Positive tests may result from superficial tinea infections.

3. No generalized allergic reactions were encountered.

4. Pityriasis rosea cannot be considered a tinea infection.

5. Intradermal tests with trichophytin are an aid in diagnosing mycoses of the glabrous skin.

114 East Fifty-Fourth Street.

301 East Nineteenth Street.

PERSPIRATION

II. THE ABSENCE OF THE ASCHHEIM-ZONDEK HORMONE IN PREGNANCY

ROBERT L. GILMAN, M.D.
AND
FRED D. WEIDMAN, M.D.
PHILADELPHIA

The fact that during pregnancy a hormone is eliminated in the urine naturally prompts thoughts to other secretions such as the saliva, sweat glands, etc. The last named are such remarkably efficient agents in preventing the elimination of certain body products and drugs [1] that the opportunity must not be lost when presented to inquire whether this extends also to hormones, particularly since the presence or absence of this hormone has been made so unequivocal of late and been so whole-heartedly accepted as a diagnostic test for pregnancy.

TECHNIC

Perspiration was collected in a rubber sheet from six colored women, all in the eighth to ninth month of pregnancy, by means of the electric light cabinet. A vulvar pad was applied to prevent possible contamination of materials by urine.

Patient	Material	Amount Injected, Cc. First Day	Amount Injected, Cc. Second Day	Total	Result
J. D.	Urine (control)	4 4 4	4 4 4	24	+
J. D.	Sweat	5 5 6	6 6 10	38	—
B. J.	Sweat	5 5 6	6 6 9	37	—
E. B.	Sweat	3 3 2	0 0 0	8	—
E. W., S. A.	Sweat, Sweat (Pooled)	10 10 10	10 10 10	60	—
H. B.	Sweat	10 10 10	10 10 5	55	—

Abundance of water was urged on the subjects, but no drugs were administered. As 100 cc. of perspiration suffices for a test, it is not necessary as a rule to prolong the sitting for more than twenty minutes. No attempt was made to segregate sweat by regions (axillary, palms and soles, etc.) in these initial tests. Specimens were filtered, and kept in the refrigerator over night.

The test involves the use of nonpregnant rabbits as recommended by Friedman; [2] the ones we employed had been kept segregated and quiet for three or four weeks.

Submitted for publication, Aug. 8, 1931.

From the Laboratory of Dermatological Research, University of Pennsylvania, and the Philadelphia General Hospital.

1. Schaffer, H. W.: Studies of Perspiration: I. Bismuth, Arch. Dermat. & Syph. **22**:624 (June) 1930.

2. Friedman, M. H., and Lapham, M. E.: Simple Rapid Procedure for the Laboratory Diagnosis of Early Pregnancies, Am. J. Obst. & Gynec. **21**:405 (March) 1931.

Whereas customary technic with urine involves dosages of but 4 cc. (intravenously three times a day for two days), the larger doses of perspiration were employed on the assumption that the animals could stand larger quantities of this less concentrated saline solution. The final reading (presence or absence of corpora hemorrhagica in the ovaries) is one of the most cleancut reactions imaginable. As a control, the urine of one of the women was similarly tested. The table will indicate the details; where small doses are indicated, it means that insufficient quantities of material were available.

RESULTS

It appears that the hormone in question was unable to pass the barrier of sweat gland epithelium; at least, it was not demonstrable under the conditions laid down for the test with urine. The effect of this is to add one more item to the list of substances incapable of passing this barrier. This outcome is regrettable as it would open the way to the comparison of apocrine and eccrine perspiration; the affinities of the former with secondary sex characteristics is naturally inviting during a state such a pregnancy. It is still possible that greater quantities of axillary sweat might still give a reaction, but in view of the total of 60 cc. employed in one of our animals, the outlook is not promising.

ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS

JOHN F. MADDEN, M.D.
ST. PAUL

Acute disseminated lupus erythematosus may be defined as an exanthematous acute disease that is characterized by the development of an erysipelas-like facial erythema and profound constitutional symptoms. In its course signs appear that have enough similarity to those of discoid lupus erythematosus to relate the syndrome definitely to the latter condition.

HISTORY

The disease was first described by Kaposi [1] in 1872. He observed a series of patients who had fever and severe toxic symptoms associated with cutaneous lesions that resembled those of erysipelas, and accordingly called the disease erysipelas perstans faceii. After prolonged observation he discovered that in some cases signs of chronic lupus erythematosus developed, and also that the reverse was true. He therefore definitely established the relationship of the two rather diverse dermatoses.

In the next twenty-five years many keen observers reported cases that confirmed Kaposi's observations. Prominent among these were Hardaway,[2] Hallopeau,[3] Koch,[4] Cavafy,[5] Boeck [6] and Sequeira and Balean.[7]

Submitted for publication, June 14, 1931.

From the Division of Dermatology and Syphilology, University of Minnesota, Dr. H. E. Michelson, director.

Read before the Section on Dermatology and Syphilology at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 12, 1931.

1. Kaposi, M.: Neure Beiträge zur Kenntniss des Lupus Erythematosus, Arch. f. Dermat. u. Syph. **4**:36, 1872.

2. Hardaway: J. Cutan. Dis. **7**:447, 1889; **10**:268, 1892.

3. Hallopeau: Wickham's Paris Letter, Brit. J. Dermat. **4**:123, 1892.

4. Koch: Arch. f. Dermat. u. Syph. **37**:39, 1896.

5. Cavafy: Brit. J. Dermat. **9**:328, 1897.

6. Boeck: Brit. J. Dermat., vol. 10, Sept., 1898; ibid., Oct., 1898; Arch. f. Dermat. u. Syph. **42**:71, 1898; Tr. Fourth Internat. Dermat. Cong., Paris, 1900, p. 188.

7. Sequeira, J. H., and Balean, H.: Lupus Erythematosus, a Clinical Study of Seventy-One Cases, Brit. J. Dermat. **14**:366, 1902.

In 1908, Pernet [8] gave an account of ten cases of acute disseminated lupus erythematosus.

In 1922, Ehrmann and Falkenstein,[9] in a characteristic and thorough résumé of the entire subject of lupus erythematosus, reviewed sixty-five definite cases of the acute disseminated type and gave a detailed account of six that they had personally observed. They felt that more than 98 per cent of cases of lupus erythematosus are associated with proved or probable tuberculosis.

In more recent times many more cases of acute disseminated lupus erythematosus have been reported or exhibited before dermatologic societies the world over. The disease has attracted the attention not only of dermatologists, but of several pathologists and internists. At a symposium held in Minneapolis in June, 1930, so eminent an internist as Professor Snapper of Amsterdam devoted considerable time to a discussion of involvement of the kidneys in this disease.

AGE AND SEX INCIDENCE

The majority of patients with acute disseminated lupus erythematosus are in the third or fourth decade of life, which is in keeping with the age incidence in chronic lupus erythematosus. The disease is comparatively rare in childhood. Brown [10] reported a lethal case occurring in a boy aged 11 years. In my series the extremes have been a boy of 5 and a man of 50 years.

All observers are agreed that females are affected far more commonly than males. No explanation of this fact has been offered. The sex of the patient does not alter the essential features of the disease or the prognosis.

ONSET

The type of onset is not consistent. Some of the patients enjoy good health up to the time when they become acutely ill; others state that their general health was below normal for some time before the malady made its appearance. Whether the first signs are cutaneous or not, the presenting symptoms, even though multiple, are persistent. From the moment the disease begins, the patient is usually aware that he is sick. Often the initial symptoms are disguised so that many incorrect diagnoses are made on the basis of the vague initial signs of acute disseminated lupus erythematosus. The clinician must be on the alert to avoid serious blunders. Because abdominal pains, nausea and

8. Pernet, George: Le lupus erythémateux aigu d' emblée, Thèse de Paris, 1908.

9. Ehrmann, S., and Falkenstein, F.: Ueber Lupus erythematodes, Arch. f. Dermat. u. Syph. **141**:408, 1922.

10. Brown, G. A.: New York M. J. **106**:931 (Nov. 17) 1917.

fever are frequently prominent, abdominal operations have been performed, with undoubted jeopardy to the patient.

Pains of a rheumatic character, general malaise, physical weakness or unaccountable fever may be among the prodromal symptoms. Goeckerman [11] emphasized the weakened state of these patients even years before the confirmed establishment of the disease.

SYMPTOMS

When the acute condition actually begins, whether it be of stormy or of insiduous onset, the symptoms are quite constant although variable in severity. The constitutional symptoms may by far overshadow the cutaneous signs, and of course eruption without systemic derangement is never found. Keefer and Felty [12] stated that the patients in their three fatal cases came to the hospital complaining of a condition other than a disease of the skin.

The following list of symptoms is the result of an effort to emphasize the important findings in the order of their frequency and importance.

Fever.—The degree of fever varies greatly with the individual case. It is always of the septic type, being especially pronounced in the more virulent cases. Hyperpyrexia is common especially in the hyperacute, fulminating cases, which terminate fatally in a rather short time. In one case observed by me (case 9) the entire course was limited to twelve days, and the temperature ranged from 103.5 to 105 F. There are usually normal periods of temperature in times of remission. One cannot estimate the severity of the case by the temperature alone. In two of our cases it did not exceed 100 F., although the patients were in a desperate condition. It may, however, be stated that hyperpyrexia accompanying a sudden severe onset usually indicates a short course with an early termination. The pulse rate is proportionate to the temperature and has no particular characteristic.

Pain.—Pain is nearly always present and is generally of the so-called rheumatic type. The muscles, bones and joints are the most frequent sites affected. As in cases 2 and 5, patients may complain of rheumatic pains long before other symptoms appear and may continue the complaint after all external signs of the disease have disappeared. One patient (case 1) had his chest strapped in order to relieve what was thought to be pleurisy. In some instances there is marked hyperesthesia, so that the weight of the bed clothes cannot be tolerated on the affected parts of the body. At times the pain is so severe that even

---

11. Goeckerman, W. H.: Lupus Erythematosus as a Systemic Disease, J. A. M. A. **80**:542 (Feb. 24) 1923.

12. Keefer, C. S., and Felty, A. R.: Acute Disseminate Lupus Erythematosus: Report of Three Fatal Cases, Bull. Johns Hopkins Hosp. **35**:294 (Sept.) 1924.

morphine will not relieve it. Some patients emphasized the fact that angina, stomatitis and pain were present in the cervical region and epigastrium.

Keefer and Felty [12] could not demonstrate any pathologic condition in the painful joints after careful roentgen studies.

Prostration.—Prostration, accompanied by profuse sweating, is extreme and out of proportion to the demonstrable findings. A severe septicemia or toxemia is suggested because of the symptoms present.

Nervous Symptoms.—At the onset the patient is noticed to be in a state of apprehension. The high degree of irritability suggests cerebral involvement of some kind. The sensorium may become clouded, the condition at times even progressing to delirium. Short periods of stupor lapsing into complete unconsciousness are common in the more severe cases. On the other hand, some patients retain a surprisingly clear mentality to the end (case 9).

Loss of Weight.—As is to be expected, loss of weight results early and is proportionate to the length and severity of the course.

Lymphadenitis.—Superficial lymphadenitis is often to be noted, especially in those regions that drain the involved skin. The inflammation in the glands does not go on to suppuration and recedes when regression of the skin lesions takes place. Goeckerman's [11] treatment is evidently based on a belief that all the deep lymphatic glands are involved.

Anorexia, Nausea and Vomiting.—These symptoms are often prominent and troublesome. Severe diarrhea may be associated with the abdominal disturbances. One patient had as many as twenty stools a day over a period of two weeks. This resulted in a marked loss of weight and suggested the presence of a severe type of colitis, but no anatomic lesions could be demonstrated, and the diarrhea ceased when a remission was effected. The same patient's first symptoms of recurrence were anorexia and nausea. Apparently the systems of certain organs are involved in particular cases. The symptoms, to be sure, are dependent on the system involved. For example, pleuritic pains in one individual or nausea and vomiting or irritability in another may suggest meningeal or cerebral effects from the noxae that are causing the disease.

Alopecia.—When present, alopecia is diffuse and secondary to the toxemia. It should not be likened to or confused with the permanent alopecia following involvement of the scalp in chronic discoid lupus erythematosus.

Cutaneous Symptoms.—The first cutaneous manifestation is frequently, but not always, on the face. The neck, hands, extremities and trunk are usually involved in the order in which they are named. The eruption begins as erythematous patches, which coalesce and cover the

entire face. The lesions are sharply demarcated; they are dusky red with a cyanotic tinge. The erythema is more or less fixed, while that noted in erysipelas is migratory. The follicular orifices are dilated and often plugged. A fine, gray, firmly adherent scale may be present. The lesions become papular, vesicular or bullous, depending largely on the amount of edema present. Rupture of the bullous lesions results in oozing and the formation of crusts. When the superficial vascular walls are injured sufficiently, hemorrhagic lesions in the form of purpura-like macules, vesicles and bullae occur.

In the less acute cases certain erythematous plaques may progress with central atrophy to simulate the typical lesion of discoid lupus erythematosus. As a rule, the eruption on the trunk and extremities is not as severe as that on the face. Here the lesions often appear as circumscribed, sharply marginated, dusky red papules or disks.

After the florid stage, the attack may subside and residual hyperpigmentation remain.

Extension is more often by the appearance of new lesions than by peripheral growth as in chronic lupus erythematosus.

The cutaneous symptoms may subside any time during the course of the disease. At death there may be no cutaneous signs remaining (case 6).

Scholtz [13] stated that the cutaneous lesions are incidental features of the whole clinical picture of pyogenic toxemia.

MUCOUS MEMBRANES

Involvement of the mucous membrane is common. The lesions are not characteristic, but are similar to those seen in exudative erythema multiforme or even pemphigus. The mucous membranes often present circumscribed or diffuse reddening, with edema, elevation, ulceration and a fibrinous membrane. Veiel [14] stated that the mucous membrane of the larynx and nose was rarely involved. Vaginal lesions were one of the most distressing symptoms in one case (case 2).

LABORATORY DATA

Changes in the blood are common. A secondary anemia accompanied by a normal leukocyte count or leukopenia is usual. Leukocytosis is rare. At the end the patient in case 6 had a leukocyte count of 350. Superimposed pneumonia or any other disease that should produce leukocytosis generally does not increase the white blood cell count. Most

13. Scholtz, M.: Lupus Erythematosus Acutus Disseminatus Hemorrhagicus, Arch. Dermat. & Syph. **6**:466 (Oct.) 1922.

14. Veiel, F.: Lupus erythematodes acutus, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1, p. 705.

of the patients with fatal cases under the care of my colleagues and me had a terminal pneumonia, but the leukocyte count was lower just before death than at any other time.

Urinary findings are more variable. Albuminuria is not a constant symptom in all cases. When present it is often accompanied by other evidences of diseased kidneys, namely, casts and red blood cells. My observations show that albumin is found more frequently in the fatal cases. It is possible that the presence of constant albuminuria may be of definite prognostic value.

Blood cultures have shown streptococci in the cases of Sibley and Wynn,[15] Gibson,[16] Low, Logan and Rutherford,[17] Seminario and Pessano,[18] Keefer and Felty [12] and others. Repeated blood cultures were made in five of my cases. Case 2 showed a gram-positive coccus in one of five cultures, case 3 Streptococcus viridans in one culture and a gram-positive coccus in three of six cultures, and case 6 Streptococcus viridans in two of four cultures. The positive blood culture may be a terminal finding and is not necessarily a proved etiologic factor.

COURSE

The usual course after the peak of the attack is recession of fever and of the eruption and improvement of the general condition. Pains in the joints and muscles and adenopathy decrease but may persist. After a few days, weeks or months there may be a new attack, with fever, reactivation of old lesions, appearance of new lesions and a return of the former symptoms. I had the opportunity of observing the patient in case 2 go through such a cycle. Exacerbations and remissions are characteristic of the disease, if the first attack is not a fatal one, and may continue for months or even years.

Patients may die after cutaneous lesions and noticeable symptoms have disappeared. In most of my examples of fatal cases the eruption became less intense shortly before death. The disease may terminate with death at any stage in its course, often rather suddenly after a period of apparent favorable progress.

The lesions of chronic lupus erythematosus occasionally become acutely inflamed; new lesions of an acute type develop, and after a period of extension gradually subside or disappear, only to reappear at some later date in the form of discoid lupus erythematosus.

---

15. Sibley, W. K., and Wynn, W. H.: Fatal Case of Lupus Erythematosus Disseminatus, Brit. J. Dermat. **35**:323 (Aug.-Sept.) 1923.

16. Gibson, F.: Fatal Case of Lupus Erythematosus, with Postmortem, Brit. J. Dermat. **37**:232, 1925.

17. Low; Logan and Rutherford: A Fatal Case of Lupus Erythematosus with Autopsy, Brit. J. Dermat. **32**:253, 1920.

18. Seminario, C., and Pessano, J.: Acute Lupus Erythematosus: Four Cases, Semana méd. **2**:721 (Sept. 4) 1930.

HISTOPATHOLOGY

The microscopic observations are not diagnostic, but are extremely suggestive.

The epidermis is often thinned to a few layers, and the papillary bodies are flattened out. In other cases the edema of the papillary body is so extreme that the epithelium is torn away and bullae arise at the site of rupture (Lewandowsky [19]). In still other cases the vesicles form within the epidermis (Reitmann and von Zumbusch [20]).

Edema is a prominent feature and involves all parts of the skin. The oozing on removal of the scale and the weeping forms are explained by the marked edema, according to Ehrmann and Falkenstein.[9]

Degenerative changes of the collagen and elastic fibers become marked early. Homogenization of the connective tissue occurs.

There is marked dilatation of the blood vessels and lymph spaces in both the superficial and the deep cutis.

There is absence of marked cellular infiltrate even in acute exacerbations. A very mild perivascular collection of round cells and a few plasma cells may be present. The infiltrate is most marked around the follicles and sebaceous glands. Gennerich [21] stated that the infiltrate is confined to the upper third of the corium.

As a rule there are no proliferative changes, and tuberculoid structure is absent.

The adnexa are comparatively free from involvement, except for the round cell infiltrate previously mentioned.

POSTMORTEM OBSERVATIONS

In three cases observed by us, postmortem examination revealed no evidence of tuberculosis. The observations were those of an acute sepsis with pneumonia.

Gennerich,[21] Gibson,[16] Grütz,[22] Sibley and Wynn [15] and Sundt [23] found no evidence of tuberculosis in their postmortem examinations.

---

19. Lewandowsky, F.: Die Tuberkulose der Haut, Berlin, Julius Springer, 1916.

20. Reitmann, K., and von Zumbusch, L.: Beitrag zur Pathologie des Lupus erythematodes acutus (disseminatus), Arch. f. Dermat. u. Syph. **99**:147, 1910.

21. Gennerich, Wilhelm: Ueber die Aetiologie des Lupus erythematodes, Arch. f. Dermat. u. Syph. **135**:184, 1921.

22. Grütz, O.: Beiträge zur Klinik und Histologie des Lupus erythematodes acutus, Arch. f. Dermat. u. Syph. **147**:524, 1924.

23. Sundt, H.: A Case of Lupus Erythematosus with Acute Exacerbation and the Appearance of Erysipelas and Phlegmon Capitis Followed by Death, with Negative Postmortem Findings as Regards Tuberculosis, Brit. J. Dermat. **38**:273, 1926.

Wail [24] and Goeckerman [11] each reported marked lymphatic tuberculosis in two cases. Bloch and Ramel [25] demonstrated microscopic evidence of tuberculosis but no macroscopic evidence of active tuberculous disease in their case.

Additional cases with tuberculous glandular involvement recognized at postmortem examination were reported by Brooke,[26] Roberts,[27] Reitmann and von Zumbusch,[20] Low, Logan and Rutherford [17] and Gardiner.[28]

DURATION AND COMPLICATIONS

The duration is one of the most variable features of the disease. Ehrmann and Falkenstein [9] observed a patient who died after one week's illness. The usual time from the onset to death is from three months to one year. Stokes [29] stated that the disease is usually fatal within five years.

The only complications that occur with regularity are pneumonia and kidney disease. Sepsis is a terminal phenomenon.

Involvement of the kidneys is often observed from the beginning, and in cases with a favorable course it may disappear. Scholtz [13] observed a patient who died from uremia after the cutaneous symptoms had involuted. Stümpke's [30] patient presented a bilateral albuminuric retinitis one month before death. A severe glomerulonephritis was demonstrated at autopsy in one of our cases.

Pneumonia is usually of the bronchial type and is often terminal. In all of our examples of fatal cases there was a terminal pneumonia. Pleurisy is occasionally noted (case 1).

Foci of infection must be removed with great caution. The removal of four abscessed teeth precipitated the fatal outbreak in case 4.

Multiple abscesses of the lung with probable pulmonary gangrene were shown by roentgen studies in case 3.

Acute colitis was the cause of death in one of Pernet's patients.

---

24. Wail, S. S.: Pathogenesis and Pathologic Anatomy of Acute Lupus Erythematosus, Arch. f. Dermat. u. Syph. **161**:43, 1930.

25. Bloch, B., and Ramel, E.: Lupus Erythematodes and Tuberculosis, Schweiz. med. Wchnschr. **32**:723, 1924.

26. Brooke, H. G.: Lupus Erythematosus and Tuberculosis, Brit. J. Dermat. **7**:73, 1895.

27. Roberts, L.: Acute Lupus Erythematosus (aigu d' emblée), Brit. J. Dermat. **33**:167, 1911.

28. Gardiner, F.: Lupus Erythematosus, Edinburgh M. J. **30**:233, 1923.

29. Stokes, J. H.: Diagnosis of Disseminate Erythematous Lupus, M. Clin. North America **10**:290 (Sept.) 1926.

30. Stümpke, G.: Zur Aetiologie des Lupus erythematodes, Dermat. Wchnschr. **82**:289, 1926.

Ravogli's [31] patient died following a subcutaneous injection of 0.001 mg. of tuberculin.

ETIOLOGY

Three schools of thought prevail in twentieth century literature concerning the etiology of acute disseminated lupus erythematosus. One group of investigators, predominately German, believe that the disease is associated with tuberculosis in a vast majority of instances. Others, notably English and Spanish observers, think that the disease is a septicemia probably due to a streptococcus. The remainder, mostly Americans, evidently favor a varied etiology. Recent literature shows an increasing trend away from the conception of tuberculosis as an etiologic agent, and a more general acceptance of one of the other views. I agree with Veiel [14] that all types of lupus erythematosus are various forms of the same disease which differ only in the severity of the phenomena present.

Inoculation of animals with material from lesions of chronic lupus erythematosus for the production of tuberculosis has given negative results repeatedly in the experience of numerous observers. However, Bloch and Ramel [25] and others obtained positive results when the inoculation was carried through three or four generations of animals. Kren and Löwenstein [32] reported 77 per cent positive blood cultures for tubercle bacilli in cases of lupus erythematosus. Inoculation of guinea-pigs, examination of sputum and autopsy observations failed to reveal tuberculosis in our patients.

Pulay [33] expressed the belief that the location of the eruption in lupus erythematosus is due to photosensitivity. He attributed photosensitiveness to certain metabolic products found in lupus erythematosus. In cases in which tuberculosis is prominent he believed that disease is due to the sensitizing action of tuberculotoxins. In a case observed by Butler and in my case 6, there was a definite history of sunburn as an initial symptom. Exposure to sunlight markedly aggravated the eruption in case 7. It seems to be well established that exposure to sunlight is a factor in the localization of the disease. The skin lesions were activated following ultraviolet ray therapy in one instance (case 6).

Acute lupus erythematosus may be due to foci of infection. The disease occurred during an attack of acute purulent maxillary sinusitis in case 8. The cutaneous symptoms immediately began to subside following drainage of the sinus. Later the sinus was occluded, and the

---

31. Ravogli, A.: Lupus Erythematosus Diffusus Unfortunately Treated with Tuberculin, J. Cutan. Dis. **33**:266, 1915.

32. Kren, O., and Löwenstein, E.: Zur Pathogenese der Tuberkulide, Dermat. Wchnschr. **92**:594 (April 18) 1931.

33. Pulay, E.: Stoffwechselpathologie und Hautkrankheiten, Dermat. Wchnschr. **73**:1217, 1921.

fever and cutaneous symptoms returned, only to disappear when drainage was reestablished. The association of abscessed teeth and of infected tonsils has been noted by many observers.

Gennerich [21] expressed the belief that the relation of this condition to tuberculosis has not been established. He stated that ferments freed by destruction of glands act as specific proteins and produce anaphylaxis. In acute disseminated lupus erythematosus there is an abundance of these ferments present in the blood, which leads to special action on the endothelium of the blood vessels and tissue cells. He believed that the facial skin is predisposed because of lowered resistance brought about by the influence of light, wind, trauma and its rich capillary supply. He explained the symmetry of the lesions on the basis of a hematogenous infection.

In more recent times Kren and Löwenstein [32] and other dermatologists of Vienna have reported a high percentage of positive blood cultures for tubercle bacilli in cases of chronic lupus erythematosus. The results of extensive studies on acute disseminated lupus erythematosus in which positive tuberculous blood cultures were obtained have not as yet been published. The recent work of Calmette and Valtis [34] on prebacillary granulemia might be a workable hypothesis for the study of these cases. An acute septic process due to tuberculosis is evidently possible, and should the tubercle bacillus be proved to be the unrefutable cause of chronic discoid lupus erythematosus, this septic prebacillary stage could well explain the acute fulminating cases of acute disseminated lupus erythematosus. To be sure, all this remains for future investigators to prove.

REPORT OF CASES

For the sake of conciseness I shall record only what I consider to be important features presented by the various patients whose cases are reported.

CASE 1.—G. B., a laborer, aged 24, first noticed a red, papular, scaly eruption on his nose in April, 1930. The eruption spread over the face, ears, neck, hands, arms and trunk during the following three months. This was accompanied by lack of appetite and a loss in weight of 17 pounds (7.7 Kg.). The patient's family doctor strapped his chest because of pain thought to be due to pleurisy. He was admitted to the University Hospital on September 19, with the symptoms described, accompanied by a temperature of 101 F. The skin of the face and eyelids became puffy. He complained of a sore throat on September 23. Pneumonia developed, and the patient died on October 3. His temperature varied from 101 to 104 F. and the fever was of the septic type. The entire picture was one of a severe toxemia or septicemia. The family history was negative for tuberculosis.

34. Calmette, A., and Valtis, T.: Filtrable Elements of Tuberculosis Virus, Ztschr. f. Tuberk. **58**:402 (Nov.) 1930.

Laboratory Data.—Albuminuria was constant and accompanied by casts and red blood cells. There was marked secondary anemia accompanied by leukopenia. Red blood cells were decreased from 3,030,000 to 1,520,000, white blood cells from 4,800 to 3,500 and hemoglobin from 70 to 43 per cent. The Pirquet and Mantoux tests were negative. The blood culture was reported to be contaminated.

Autopsy.—Generalized icterus was present. The peritoneal cavity contained 100 cc. of clear fluid. There was bilateral lobar pneumonia. No evidence of tuberculosis was obtained on gross or microscopic examination.

Case 2.—P. P., a waitress, aged 20, stated that she noticed colicky abdominal pains followed by nausea and vomiting in July, 1929. She spent two months in a hospital at that time, but the pain continued. It was accompanied by loss of weight, nervousness, weakness and inability to retain food. In November, 1929,

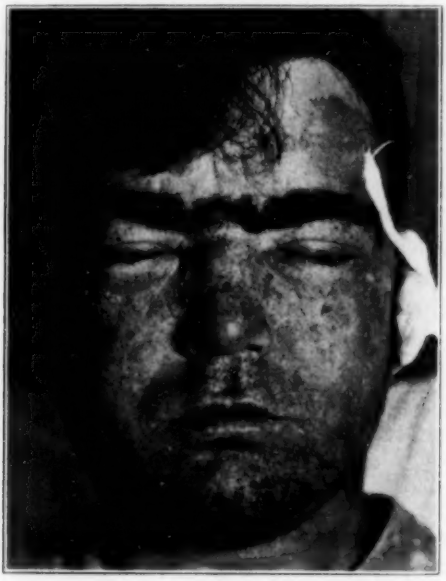

Fig. 1 (case 1).—Acute, diffuse edema with exudation in case with fatal outcome.

the patient had lost 40 pounds (18.1 Kg.). She was operated on in March, 1930, by a private physician for appendicitis. No relief from pain was experienced. In May, 1930, she was admitted to the University Hospital because of tingling and pain in her legs, incontinence and delusions, in addition to her previous complaints. She presented on admission a swollen red tongue, an ulcer on the buccal mucous membrane and lesions on her face that were called "acne." The patient was first seen by the dermatologic staff on July 10, 1930. She then presented a brownish pigmentation of the skin of the face, neck, hands and arms. The skin was very dry and covered with fine scale, and the follicular orifices were dilated and plugged. There were exudative, bleeding, crusted, reddened patches and ulcers covered with a grayish membrane on the buccal and vaginal mucous membranes. The patient was having as many as twenty stools a day. The case was demonstrated by Dr. Snapper of Amsterdam as one of acute disseminated lupus erythematosus.

In August, 1930, the pains in the legs became so severe that the patient could not stand the weight of the bed clothes. Her ankle and wrist joints became swollen and very painful. A diffuse alopecia developed in September, 1930 In October, 1930, the patient was thought to be dying. She had lost 84 pounds (38 Kg.) in fifteen months. Small doses of gold sodium thiosulphate intravenously injected were alternated with small doses of neoarsphenamine at five day intervals. The patient weighed 75 pounds (35.4 Kg.) and was discharged on Dec. 15, 1930. The family history was negative for tuberculosis.

Laboratory Data.—Albuminuria was present at half the examinations. There was secondary anemia accompanied by a leukocyte count varying from 6,400 to 9,600. Blood culture was positive in one of five examinations. A gram-positive coccus was found. The results of biopsy were characteristic of acute disseminated lupus erythematosus.

Fig. 2 (case 2).—Pellagroid distribution of lesions.

Additional Data.—The fever was constant and septic; the temperature ranged between 98 and 100 F.

The pains in the muscles and joints persisted. The patient gained 38 pounds (17.2 Kg.), weighing 116 pounds (52.6 Kg.) in April, 1931. At this time the rheumatic pains became more severe. She became nauseated and was unable to retain food. At the time of this report, May, 1931, an exacerbation appears to be developing. The pains have increased; she cannot retain food, vomits frequently, and has lost 5 pounds (2.3 Kg.) during the past week (May 15, 1931).

Case 3.—J. T., a laborer, aged 50, had what he described as a dusky red face, hands and arms during the summer of 1929. There were no subjective symptoms. During the summer of 1930, new lesions appeared on the legs, and he noticed a burning sensation in all the involved areas. His face and eyelids became swollen in April, 1931. This was accompanied by fever and a loss of 10 pounds (4.5 Kg.)

in weight. About two weeks later dysphagia and hoarseness developed. The patient could not swallow solid food; paroxysms of coughing occurred, and about one cupful of sputum was expectorated each day. The skin over the face, hands, arms, upper part of the trunk and legs presented a diffuse, dusky red erythema. The lesions on the body resembled those of poikiloderma atrophicans vasculare. The skin was dry, edematous and covered with a fine scale. The follicles were open-mouthed and presented plugging. The temperature varied from 98.6 to 100 F. The family history was negative for tuberculosis.

Laboratory Data.—There was secondary anemia accompanied by a leukocyte count at the upper limits of normal. The cell count showed: red blood cells, 3,500,000; hemoglobin, 76 per cent, and white blood cells, 9,600. The sputum was repeatedly negative for tubercle bacilli. The urine exhibited a slight trace of

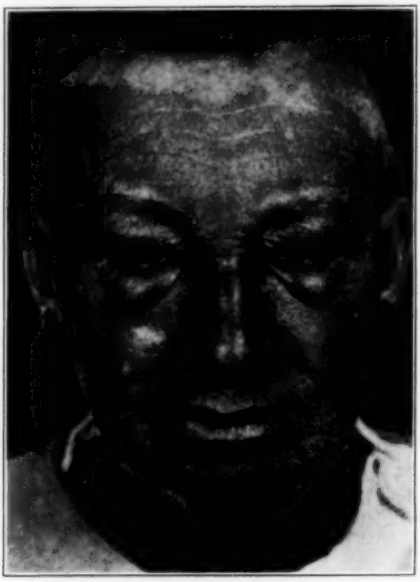

Fig. 3 (case 3).—Extreme edema and the dusky red, cyanotic tinge of the erythema. Note the sharp line of demarcation on the forehead.

albumin at about half the examinations. The Pirquet and Mantoux tests were negative. Blood cultures exhibited Streptococcus viridans in one culture and a gram-positive coccus in three of six cultures taken. X-ray films showed multiple pulmonary abscesses and probable gangrene of the lung. There were no evidences of tuberculosis. The results of biopsy were characteristic of acute disseminated lupus erythematosus.

Additional Data.—The patient died in August, 1931.

Autopsy.—There were a carcinoma of the stomach and multiple metastases in the lungs. No evidence of tuberculosis was obtained on gross or microscopic examination.

Case 4 (Dr. S. E. Sweitzer's case).—Mrs. G. M., a housewife, aged 34, was admitted to the University Hospital in August, 1919, complaining of pain in the left side of the neck, edema of the eyelids and an eruption on the face. She stated

that she first noticed red, scaly spots over the bridge of the nose in June, 1918. The eruption remained stationary for eleven months. In July, 1919, four teeth were extracted. Immediately the eruption spread over her entire face, her eyelids became swollen, and she experienced extreme pain in the neck. This was accompanied by marked stomatitis. Severe pyorrhea had been present for years. The temperature was septic and sometimes reached 104 F. The patient was irrational at times. The lower part of both legs became covered with reddened, indurated patches. In October, 1919, the patient became very toxic, was often delirious, and constantly complained of rheumatic pains in the legs. A diffuse alopecia was present, and the remaining hair was dry and lusterless. She died on November 1 from a terminal bronchopneumonia. The family history was negative for tuberculosis.

Fig. 4 (case 4).—Erythema multiforme-like eruption with lesions on lips. Note the less active lesions on the neck.

Laboratory Data.—Albuminuria was present at every examination, accompanied by hyaline and granular casts, red blood cells and pus cells. The sputum was repeatedly negative for tubercle bacilli. Secondary anemia associated with leukopenia was present. The red blood cells were decreased from 5,240,000 to 2,240,000, and the white blood cells from 5,742 to 3,150. Inoculations of guinea-pigs for tuberculosis and blood cultures were repeatedly negative.

CASE 5 (Dr. C. D. Freeman's case).—Miss C. L., a clerk, aged 28, was admitted to the hospital in August, 1923, complaining of anorexia, loss of weight, weakness and pains in the arms and legs. The family history was negative for tuberculosis. The patient stated that she noticed pains in her joints during the winter of 1922 and 1923. These pains became progressively more severe. In June, 1923, she tired easily and became very weak. During July, 1923, her face became dull red, her hair fell out, and she lost a great deal of weight. Three teeth were

extracted with no noticeable effect. The eruption spread to the neck, hands and arms in August, 1923. She had lost 37 pounds (16.8 Kg.) in weight at that time. The skin over the entire face, neck, hands and arms was dry, pigmented, dull red, rough and covered with a fine scale. The follicles were dilated and plugged. In September, 1923, the eruption involved the trunk. Nausea and vomiting occurred at that time. The patient became progressively worse, and died at home during the winter of 1923 and 1924.

The temperature was septic and ranged from 99 to 103 F.

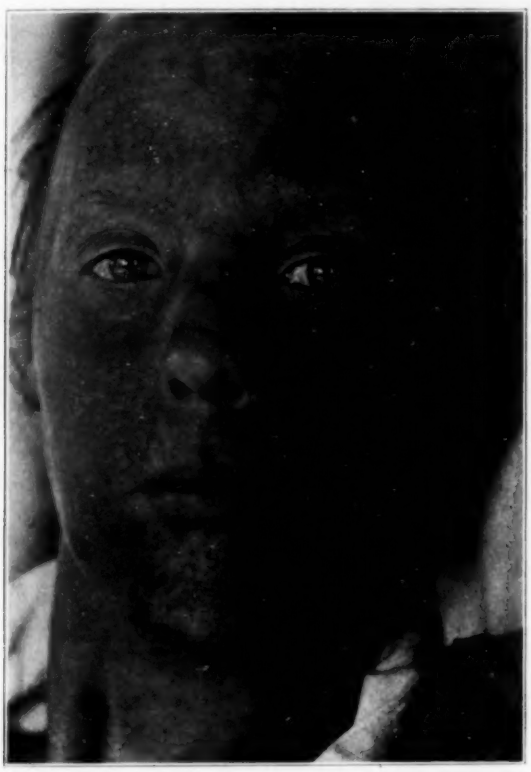

Fig. 5 (case 5).—Pigmentation following an acute attack.

Laboratory Data.—Albuminuria accompanied by casts, red blood cells and pus celis was present. A secondary anemia associated with leukopenia and a normal leukocyte count persisted. The red blood cells were decreased from 4,750,000 to 3,700,000, and hemoglobin from 80 to 52 per cent, and the white blood cells were increased from 3,700 to 7,600. Three blood cultures were negative.

Case 6 (Dr. H. E. Michelson's case).—Miss A. T., a university student, aged 20, was admitted to the University Health Service in May, 1924, complaining of sore throat and mouth. She stated that the eruption appeared after a severe sunburn. The family history was negative for tuberculosis. She presented bright red, infiltrated, raised patches over the bridge of the nose. The gums and buccal mucous membranes were red and swollen. The cervical lymph nodes were enlarged and

tender. Sharp epigastric pain developed. The patient was transferred to a sanatorium in June, 1924, and was given general ultraviolet ray therapy. The eruption immediately spread to the shoulders and trunk. Phlebitis of the left leg developed. In October, 1924, the patient presented generalized lymphadenitis, diffuse alopecia, a puffy face and marked edema of the eyelids, accompanied by a purulent discharge from the right ear. In December, 1924, ascites was present. The patient was delirious most of the time. The cutaneous symptoms disappeared. She became more toxic during the month, and died on Dec. 12, 1924.

The temperature was septic and ranged from 99 to 103 F.

Laboratory Data.—A secondary anemia accompanied by leukopenia was present. The leukocyte count ranged from 4,000 on May 19, 1924, to 1,200 on November 28 and to a final count of 350 on Dec. 4, 1924. Albuminuria and casts were present in large amounts at all examinations. There was no reaction to 10 mg. of tuberculin. Two of four blood cultures taken were positive for Streptococcus viridans.

Autopsy.—Postmortem examination revealed an ulcerative endocarditis involving the tricuspid valve, healed rheumatic endocarditis, embolic glomerulonephritis,

Fig. 6 (case 7).—Characteristic lesions on hands. Note the sharply demarcated, dusky red, erythematous patches.

gangrenous tonsillitis and hemorrhagic centers in the lobules of the liver. No evidence of tuberculosis was found.

Case 7 (Dr. H. E. Michelson's case).—Mrs. M. O., a housewife, aged 33, first noticed small red, elevated patches on the face in May, 1927. These soon became confluent and spread to the neck, hands and upper part of the chest. The patient felt that the eruption was definitely aggravated by sunlight. On her admission to the University Hospital in November, 1927, the involved areas were edematous, beefy red, indurated and tender on pressure. The patient had severe pyorrhea. Her family history was negative for tuberculosis. The temperature ranged from 98 to 101 F. and was septic. She was discharged during a remission of the condition, on Dec. 5, 1927. She was seen about one year later by Dr. Michelson, at which time she still remained in good health.

Laboratory Data.—Urinalysis gave negative results. A slight secondary anemia accompanied by a normal leukocyte count was present. The cell count showed: red blood cells, 4,090,000; hemoglobin, 75 per cent, and white blood cells, 7,150.

Case 8 (Dr. H. E. Michelson's case).—R. S., a boy, aged 5 years, presented lesions of acute disseminated lupus erythematosus on the face and hands. His

temperature was septic and reached 105 F. Examination revealed an acute, purulent maxillary sinusitis. The sinus was drained, and the cutaneous symptoms immediately began to subside. Later the sinus was occluded, and the fever and cutaneous symptoms returned, only to disappear when drainage was reestablished. The patient was exhibited at an annual meeting of the Minnesota Dermatological Society, and the diagnosis was concurred in by all the members present.

CASE 9 (Dr. H. E. Michelson's case).—Miss K., aged 47, was entirely well until February, 1930. Her illness was characterized by a severe erythematosus eruption on the face, hands and chest. There was a high degree of stomatitis and angina, as well as membranous lesions in the vagina. The prostration was pronounced from the beginning. The lesions on the face soon became bullous, giving the appearance of a second degree burn. The patient was examined by an internist; there was no clinical evidence of pneumonia or endocarditis. The eruption spread over the entire trunk. The temperature hovered around 105 F. The patient died on the twelfth day of the attack. There was no autopsy.

Laboratory Data.—The blood culture was contaminated. The urine showed albumin, red blood cells and casts.

DIAGNOSIS

The diagnosis is made by careful consideration of the constitutional and cutaneous symptoms.

In differential dermatologic diagnosis one must consider extensive disseminated chronic lupus erythematosus, erysipelas, pellagra and erythema multiforme.

Disseminated chronic lupus erythematosus presents early in its course one or more reddish, sharply demarcated, papules varying in size from that of a pea to that of a bean. These are covered with a grayish, firmly adherent scale. The initial lesion enlarges peripherally, and in the course of months or years may assume the size of a coin or become much larger. The lesions are well defined in outline and are usually pink. The shape is generally round, oval or irregular from the junction of progressing patches. The border is redder than the rest of the lesion and sharply demarcated. The center is depressed, paler and covered with an adherent scale; later it may present atrophy and scarring. The follicular openings are dilated and may be plugged. Signs of acuteness are absent.

The eruption in erysipelas first appears at a given point, from which the disease progresses. It commonly begins as a patch of varying size, which is edematous, fiery red, slightly elevated, irregular in outline, sharply circumscribed and without peripheral islands. The lesion has a peculiar smooth, shining, glazed appearance. The patient may complain of heat, pain, itching or burning. The color fades under pressure. The affected area is tender, moderately firm and perceptibly hotter than normal. In some cases in which the exudation of serum has been rapid, vesicles and bullae appear.

Pellagra often begins as large macules, light or dark red, which soon fuse, forming a patch of dermatitis almost identical in appearance with

that caused by the sunlight. As the disease progresses, the color deepens and becomes reddish brown. Later desquamation begins. The lesions then present a roughened, scaly surface. Early in the process there is moderate swelling. In more acute cases bullous lesions may develop on an erythematous base, drying in a few days, and leaving a thickened, crusted epidermis. Secondary pyogenic infection may follow in the vesicular and bullous types. In severe cases ulceration and fissuring may take place. The lesions are always well defined. The skin may be pigmented after the eruption disappears. After several attacks the skin becomes more or less permanently pigmented, roughened, dried, thickened, hardened and scaly. The terminal stage is exhibited as a thin, cicatriciform, parchment-like integument, presenting striae parallel with the long axis of the hand. The lesions are most often found on the exposed areas of the body. The dorsa of the hands and the wrists, face, neck, feet and ankles are commonly involved.

Erythema multiforme nearly always presents a symmetrical eruption, which is usually found on the dorsa of the hands and feet, on the legs and the forearms and often on the face and neck. While multiformity is the rule, one type of lesion usually predominates in each case. The most common lesions are edematous-looking macules, flattened papules and large flat nodules. Occasionally vesicles and bullae are present. The eruption usually begins with dark or purplish-red macules ranging in size from that of a pinpoint to that of a dime, which in the course of some hours exhibit tumefaction in various degrees, thus producing the papules, nodules and other lesions previously mentioned. The disease usually runs its course in from two to four weeks. Recurrent attacks are not uncommon. The lesions occur in different shapes, sizes and colors. Peculiar shades of reddish black, purplish blue, red, yellow, orange, black and blue are exhibited.

Other dermatoses might be considered, but they are so irrelevant that it hardly seems necessary.

The dermatologic diagnosis of acute disseminated lupus erythematosus offers no great difficulties. The fixed erythema, its peculiar cyanotic tinge and its prevalence on the exposed parts of the body, coupled with profound constitutional symptoms, are the criteria for decision.

THERAPY

Gold compounds, irradiation of the deep gland-bearing areas (Goeckerman[11]), repeated transfusions, intravenous injections of streptococcic vaccine and quinine have been used with varying results.

Our patient (case 2) had been considered moribund for approximately three weeks when very small doses of gold sodium thiosulphate were started. She showed immediate improvement. After five injections of 10 mg. of gold sodium thiosulphate and a like number of

injections of 1 decigram of neoarsphenamine given alternately at five day intervals, she was discharged from the hospital. This treatment was continued less frequently for two months, during which time the patient was without symptoms. At the time this article is written, two months later, a definite exacerbation of the former symptoms is developing. Two other patients (cases 1 and 3) were treated with gold compounds with no improvement.

Foci of infection should be removed with great caution. The extraction of four abscessed teeth caused a fatal attack in case 4. Drainage of an infected antrum cured the patient in case 8.

Exposure to actinic rays should be avoided when possible. Sunburn was the initial symptom in two of the cases reported. Ultraviolet rays caused a definite aggravation of the condition in case 6.

We must conclude that there is no specific therapy for the disease. When a definite focus of infection is found it should be removed cautiously.

PROGNOSIS

The prognosis is uniformly bad, but apparently not hopeless. The cures reported in the literature are generally of too short duration to be taken at their face value. Subsequent histories are not given for most of the patients. The case of von Zumbusch,[35] observed over a period of years, was an exception in which the outcome was favorable. The patient who recovers is truly a rare exception.

CONCLUSIONS

1. Acute disseminated lupus erythematosus is an important clinical entity.

2. The symptoms are more or less constant, but the degree of severity varies greatly. Constitutional symptoms may completely overshadow the cutaneous symptoms.

3. Albuminuria was a constant finding in the fatal cases reported. Its presence may be of definite prognostic value.

4. In fatal cases leukocytosis does not develop, even when conditions arise in which it would be expected.

5. The histopathology is not an important diagnostic aid, but is suggestive and worthy of study.

6. The disease has the characteristics of a septicemia or toxemia.

7. Streptococci have been repeatedly reported to be present in the blood stream.

8. Tuberculosis has not been proved to be an etiologic factor in many instances, but the newer work must be evaluated before tubercle bacilli are excluded as a probable cause.

---

35. von Zumbusch, L.: Zur Aetiologie des Lupus erythematodes, Arch. f. Dermat. u. Syph. **149**:136, 1925.

9. There is no specific therapy

10. The prognosis is grave, even when there is apparent recovery, for relapses are the rule.

ABSTRACT OF DISCUSSION

DR. JOHN H. STOKES, Philadelphia: Dr. Madden's paper is an excellent summary and review of an important subject. I can only add or reemphasize a few points. Disseminated lupus erythematosus may progress to a fatal outcome with cutaneous signs so slight or so confusing as to fail of recognition. I have seen dermatologic diagnoses of acute eczema and medical diagnoses of typhoid fever with a negative Widal test. Libman's syndrome of facial lesions with subacute bacterial endocarditis is a most interesting relative of disseminated lupus erythematosus. The lesions of the mouth in acute lupus erythematosus should not be overlooked. The silvering of the vermilion border on a livid base, the red or livid macules about the finger-tips and the peculiar cyanotic tinge of the whole eruption mentioned by Dr. Madden are all especially important diagnostically. While the leukopenia may be startling, a survey of our cases made by Dr. Garner indicated, to my surprise, for I had always emphasized this symptom, that it is not crucial in diagnosis. It may be enlightening, especially in those cases in which impending dissemination is suspected, but often it is not so. Dr. Madden has well portrayed the differences in opinion as to etiology. To my mind, the victim of acute disseminated erythematous lupus is first and foremost an allergic person explosively and furiously responsive to his infection and with a broken or inhibited leukocytic defense. The tuberculous and the septic factors are both undoubtedly present, sometimes the one, sometimes the other being more prominent. Ravogli, I think it was, pointed out years ago the fatal effect that tuberculin even in minute doses may have on these patients, and the extraction of a single infected tooth in an acute case may cause coma for days.

Therapeutically, the use of gold preparations offers something new and helpful but, in my experience, as in Dr. Madden's, perhaps only temporarily effective. Jadassohn commended plasmochin to me as sometimes preferable to quinine in the large doses required.

DR. H. J. TEMPLETON, Oakland, Calif.: Dr. Madden's paper and Dr. Stokes' discussion bring to my mind two cases. One was that of a man, aged 40, who first noticed patches of discoid type on his cheeks following extirpation of a tooth. There had been no previous evidence of disease. On roentgen examination, I found that eight or ten teeth showed abscesses, and advised their extraction one at a time. An enthusiastic dentist pulled them all at once, and a generalized lupus erythematosus developed. Fortunately, the dentist had preserved the teeth. A vaccine was prepared after Streptococcus hemolyticus was recovered. This vaccine was administered intradermally, and, although the patient spent four months in the hospital at Oakland, he finally recovered.

Another case was seen in a patient of Dr. Harry Alderson who developed lesions of discoid type following a gum boil. The lesions did not remain discoid, but spread, and Dr. Alderson referred the patient to me, as she lived on my side of San Francisco Bay. We thought the teeth caused the trouble, but feared extraction, although we finally advised it. Again, Streptococcus hemolyticus was recovered, a vaccine was prepared, and after some time in the hospital this patient also recovered. Whether the recovery occurred because of the vaccine or in spite of it I am not prepared to say. I believe some of the cases are streptococcal in origin, and it is possible that desensitizing therapy may be of some value.

Dr. Hamilton Montgomery, Rochester, Minn.: Lupus erythematosus must be regarded as a systemic disease, especially in its disseminate forms. All gradations between the chronic discoid and the acute disseminate types are seen both clinically and histopathologically. The etiology of the disease is not known. Ramel's work regarding an attenuated form of tuberculosis requires confirmation. As a working hypothesis the disease may be regarded as affecting the reticuloendothelial system with special affinity for the skin and lymphatic glands, giving rise to toxic disturbances in the body, decreasing the powers of resistance to several other infections (particularly streptococcal and tuberculous) and increasing the susceptibility of the skin to external and internal influences. Systemic manifestations in disseminated lupus erythematosus are multiple and varied and may predominate over the cutaneous manifestations. Among these the following frequently occur: pyrexia with a septic type of temperature simulating typhoid fever or malaria, leukopenia and secondary anemia, abdominal symptoms simulating those of cholecystitis and appendicitis, albuminuria and evidence of nephritis, myocarditis or endocarditis, arthritis and, at times, evidence of overwhelming infection of streptococcal or tuberculous etiology.

The histopathologic picture in lupus erythematosus is similar in both the acute and the chronic types. Whereas the earliest changes are nonspecific, within a few weeks or months characteristic changes occur in the epidermis and cutis the combination of which may permit a definite diagnosis. If, therefore, a lesion is selected for biopsy that has been present a month or more and has not been subjected to local therapy, the histopathologic picture may be of great value in helping to establish the diagnosis of lupus erythematosus disseminatus.

In the literature internists point out cases with transitory erythema associated with myocarditis and endocarditis of bacterial or nonbacterial origin, abdominal symptoms and arthritis, and call them cases of acute disseminated lupus erythematosus. I feel that such cases should be kept at the side for the time being. just as some of the true cases of erythema facei perstans of Kaposi probably should not be included with those of lupus erythematosus disseminatus, as the lesions never show atrophy or keratotic plugging or other features of the latter disease. Finally, lupus erythematosus disseminatus may at times show vesicular and bullous lesions but should not be confused with the diseases in the pemphigus-lupus erythematosus group of Senear and Usher, which I believe are pemphigus.

Dr. Clark W. Finnerud, Chicago: Dr. Madden has given a most accurate and detailed resumé of the facts concerning this disease. He was fortunate enough to obtain necropsy studies in three of the nine carefully studied cases, a method of approach that is of utmost importance in adding to our knowledge of the pathogenesis of this disorder. To me it is not surprising that in not one of his cases, regardless of whether necropsy was performed, was there demonstrable evidence of active tuberculosis. These findings are in accord with those in many such cases that have come to necropsy since the time of Ehrmann's review of the subject. In my own experience three patients came to necropsy, and active tuberculosis was demonstrated in but one of them.

It seems to me most logical to consider acute disseminated lupus erythematosus as a toxic process, possibly the result of an infectious agent, a process that is capable of lowering the patient's resistance to such a point as to make him susceptible to infections of various types, tuberculosis being merely one of many, which occur intercurrently and terminally with this disease.

Dr. Samuel Ayres, Jr., Los Angeles: One point that Dr. Madden brought out is interesting, namely, the fact that the only patient in this group who recovered

was the one with acute sinus infection, which cleared up with drainage of the sinus; when the sinusitis again flared up, the disorder recurred and again cleared up when the sinus was drained. I agree with Dr. Templeton that the condition probably represents an allergic reaction to certain infections. I also agree with his caution in the matter of removing infected foci, such as the removal of one tooth at a time. Certainly when a person has a disease that is 100 per cent fatal it seems important to remove all foci that may be found. I think his method of desensitizing is very valuable. It might be valuable also to make skin tests with bacterial extracts obtained from foci of infection to determine whether the patient is actually hypersensitive to the organism in question. I feel that many of the cases undoubtedly are due to sinus infection because of the frequence of symptoms referable to the sinuses. In the nasal infections there is one group, frequently overlooked not only by the dermatologists but by many nose and throat specialists, in which it is not always possible to detect the condition by symptoms of pain, or even by transillumination. A patient may have a severe sinus infection without giving much evidence by transillumination. Such cases can often be detected only by careful roentgen examination and irrigation. I think one should be careful about thorough investigation in all these cases.

Dr. Fred D. Weidman, Philadelphia: I wish to put on record another case in which necropsy was performed which I saw in its incipiency when the patient was in the general medical wards with arthritis. The necropsy observations did not reveal any evidence of tuberculosis. I dare say that when the chapter on lupus erythematosus is fully written it will be somewhat like that on erythema multiforme as we know the latter condition today. About twenty-five years ago Osler reported a large series of cases of what he called erythema multiforme—multiform in that (at yearly intervals, or perhaps with remissions of many years) the eruption might at one time be purpuric, at another time urticarial, or at still another the classic erythema multiforme of the dermatologist. In some cases there often was arthritis, and in others irritation of the gastro-intestinal tract. I dare say that in lupus erythematosus the same variation will prove to exist. I believe that lupus erythematosus disseminatus is not an etiologic entity, but that many factors can produce it; this case in which necropsy was performed indicates that arthritis is one of the causative conditions that belong in the list.

Dr. Michael H. Ebert, Chicago: Dr. Madden has presented a large series of cases of lupus erythematosus and has given an excellent survey of the subject. He emphasized that whatever may be the presenting manifestation of the disorder that particular manifestation seems to continue throughout, and I wish to report briefly two cases in which the presenting symptom was neuritis.

Both patients were women. One was observed for a considerable time by competent physicians without any diagnosis being made except that of peripheral neuritis, and without discovering any cause for the condition. The other woman had been under the care of a neurologist for a year, a diagnosis of neuritis having been made. In both cases the condition eventuated into classic lupus erythematosus disseminatus, and throughout the course of the disease continued to present the symptoms of peripheral neuritis.

Dr. Max S. Wien, Chicago: There was a patient under observation at Cook County Hospital in Chicago in whom necropsy revealed no evidence of tuberculosis, but changes in the mediastinal glands of the Dorothy Reed-Sternberg type.

NORMAL PIGMENTATION IN THE NAILS OF THE NEGRO

SAMUEL MONASH, M.D.
NEW YORK

I have found no record of a systematic study of pigmentation of the nails in the Negro. Heller,[1] in his comprehensive work on the nails, referred principally to communications on this subject by Ochs [2] and Templeton.[3] Ochs' patient was a Negress, 37 years old, who had on all the finger-nails parallel, pigmented, longitudinal stripes, which were present from birth.

Templeton [3] described a pigmented longitudinal stripe occurring on the nail of the fourth finger of the left hand in a Negress of 28. It had been noticed first as a dark spot near the root of the nail nine years before, and had gradually extended out toward the free edge, increasing somewhat in width in the last two years. The pigment was shown to be in all probability melanin, and Templeton considered the pigmented stripe a nevus. He stressed the rarity of the condition, for which reason he reported the case. I disagree with Templeton both as to the nevoid character of the pigmentation and as to its rarity.

This study is based on examinations of the finger-nails of 296 Negroes, who varied in age from a few days to 62 years. The toe-nails were not examined systematically, but it can be stated that pigmentation of the toe-nails tends to parallel pigmentation of the finger-nails. It is of the same type and follows the same general rules that were found to be true for pigmentation of the finger-nails. In addition to the examination of the nails, the degree of pigmentation of the skin was noted by means of the color top method, devised by Todd and van Gorder [4] and used by Barnes [5] in a study of the inheritance of pigmentation in the Negro. The top is called the "pupil's color top" and is manufactured by the Milton Bradley Company of Springfield, Mass.

Submitted for publication, July 6, 1931.

From the Department of Dermatology, College of Physicians and Surgeons, Columbia University, and the Stuyvesant Square Hospital, formerly the New York Skin and Cancer Hospital.

1. Heller, J.: Krankheiten der Nagel, Berlin, Julius Springer, 1927.
2. Ochs, B. F.: J. Cutan. Dis. **32**:238, 1914.
3. Templeton, H. J.: Pigmented Stripe in the Nail, Arch. Dermat. & Syph. **14**:533 (Nov.) 1926.
4. Todd, T. W., and van Gorder, L.: Am. J. Phys. Anthropol. **4**:244, 1921.
5. Barnes, I.: Human Biol. **1**:321, 1929.

In view of the varying degrees of color in different parts of the Negro's skin, it is advisable to use similar regions for the determination. In this work the skin on the outer aspect of the upper arm was examined.

To convey a rough idea of the shades that are represented by the figures obtained in this way, one can say that 35 per cent is a shade of tan; as the figure increases, the color becomes brown, with 70 per cent representing a dark brown; 80 per cent is brownish black, and 85 per cent is a deep brown black. Barnes [5] found that the average skin pigmentation of the New York Negro determined by this method was 70 per cent.

Fig. 1.—Pigmentation of the nails, showing the longitudinal stripes running the length of the nails.

Fig. 2.—Pigmentation of the nails.

TYPE OF PIGMENTATION

Pigmentation of the nails usually occurs in the form of longitudinal stripes running the length of the nail, as is well shown in figures 1 and 2. On each nail there may be single or multiple stripes, and they may vary in width from a thin line to several millimeters. They vary in depth of color in different persons, being generally darker in the darker Negroes. They may be present in any portion of the nail, but usually occupy the central area or the lateral margins. There is no deeper pigmentation of the nail bed under these pigmented stripes. In the darker Negroes, those with a shade of 80 per cent or more, there is usually in addition a macroscopically visible diffuse pigmentation of the entire nail substance, even in those portions not showing longitudinal striping.

Microscopically, the pigmented granules are found to be scattered through the entire thickness of the nail substance, with a tendency for the deeper layers to be more pigmented than the superficial. There is

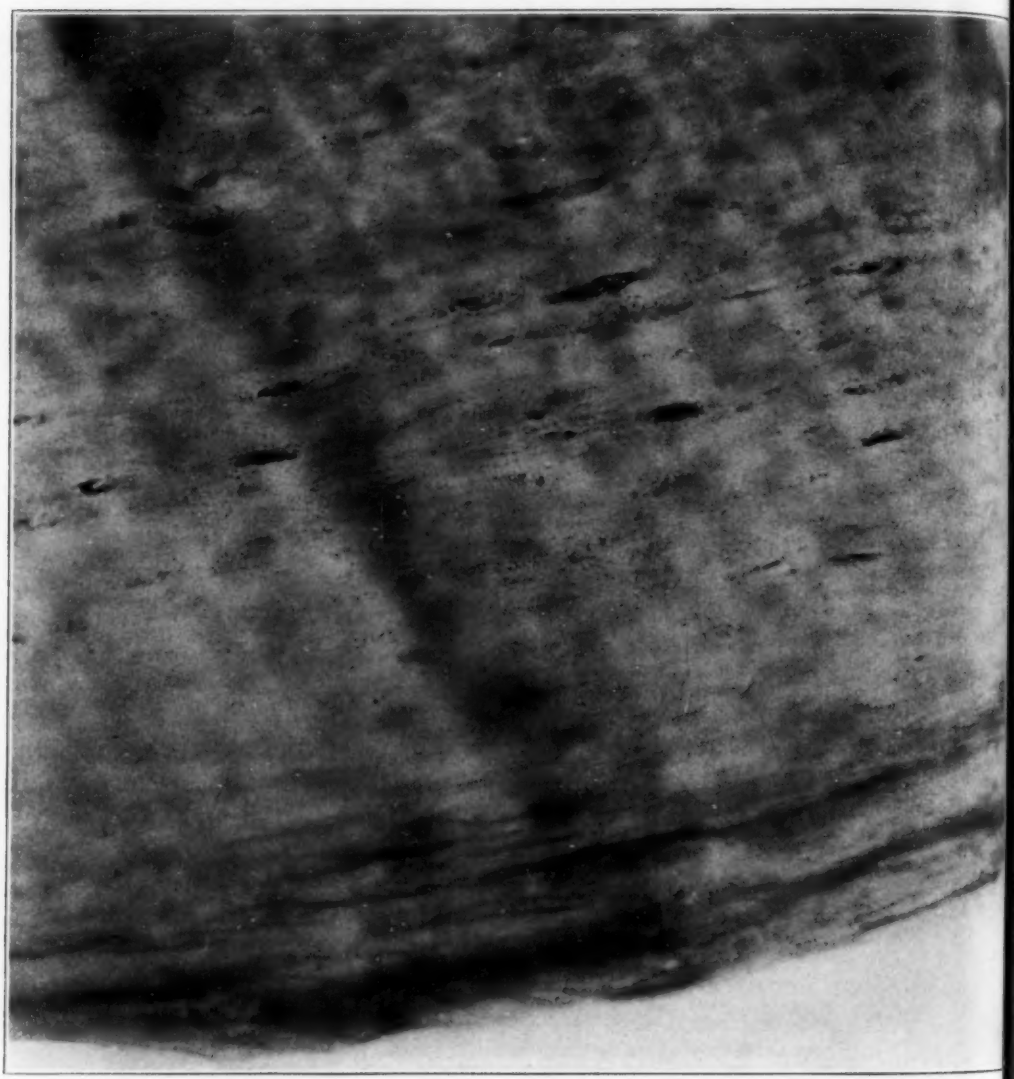

Fig. 3.—Photomicrograph, showing the pigment granules taking the form of the nail cells.

a definite concentration of the pigment in the areas corresponding to the pigmented stripes. The pigment granules take the form of the nail cells and undoubtedly owe their color to the presence of melanin (fig. 3).

RELATIONSHIP OF PIGMENTATION TO AGE

No pigmented nails were observed in children at birth, the earliest case being that of a boy, 2 years and 9 months of age. The lack of pigmentation at birth may be attributed to the general paucity of pigmentation in Negroes at that age. I do not doubt, however, that if a sufficient number of very darkly pigmented children are systematically examined, several will be found to have pigmented stripes in the nails at an earlier age than that of the boy mentioned.

Excluding the children of 10 days or under, the series comprises 66 children below the age of 10 years. Of these 15, or 23 per cent, showed pigmented stripes. From the ages of 10 to 19, inclusive, there is a total of 104, of which 42, or 40 per cent, had pigmented stripes. In the third decade, from 20 to 29, inclusive, the total is 35, of which 24, or 70 per cent, had pigmentation. In the fourth decade and older, of a total of 69, 37, or 53 per cent, had pigmented stripes.

A more accurate estimation of the relationship of age to this type of pigmentation is secured by eliminating from consideration those Negroes with a skin pigmentation of less than 65 per cent, since below this figure, nail pigmentation is not common. By so doing, in the first decade, from birth to 9 years, inclusive, of 50, 15, or 30 per cent, were pigmented; in the second decade, of 81, 42, or 52 per cent, were pigmented; in the third decade, of 32, 24, or 75 per cent, were pigmented; above the age of 30, of 44, 37, or 88 per cent, were pigmented.

One arrives at similar conclusions and secures additional information by examining the number of darker Negroes, namely, those with a shade of 80 and 85 per cent, showing pigmentation of all the finger-nails of both hands. In the first decade, of 9, there was 1, or 11 per cent; in the second decade, of 22, there were 3, or 14 per cent; in the third decade, of 8, there were 3, or 37 per cent; in the age group of 30 and over, of 18, there were 10, or 55 per cent.

The foregoing data show that (1) pigmented stripes in the finger-nails may begin to appear at any age; (2) there is a progressive increase in the occurrence of pigmented stripes with increasing age, and (3) there is a tendency for more nails to be involved with increasing age.

RELATIONSHIP OF NAIL TO SKIN PIGMENTATION

In those Negroes with a skin pigmentation of less than 65 per cent, nail pigmentation is infrequent. In the group of 89 subjects, only 3, or 4 per cent, had pigmented stripes. In the group with a skin pigmentation of 65 per cent or over, there were 207, of which 118, or 57 per cent, showed pigmented stripes.

If one subdivides the latter group into two divisions, namely, one with a skin pigmentation of 65, 70 and 75 per cent and the other com-

posed of the darker Negroes, namely, those with a pigmentation of 80 and 85 per cent, the relationship of skin and nail pigmentation becomes also apparent. In the lighter group, of a total of 148 persons, 71, or 48 per cent, showed striped nails; in the darker group, of 59 persons, 45 or 76 per cent, showed the same changes.

In the age group of 20 years and over, those of 80 and 85 per cent skin pigmentation showed pigmented stripes in practically every case. This is shown by the fact that of 27 persons in this group, 26, or 96 per cent, showed these changes.

The conclusion can therefore be reached that there is a definite relation between skin and nail pigmentation, and that with increasing skin pigmentation there is a definitely increased nail pigmentation.

DISTRIBUTION OF PIGMENTED STRIPES

The first nail to become pigmented is usually that of the thumb or first finger, and the pigmentation usually proceeds in regular order, the second, third, fourth and fifth fingers following in sequence. This rule is, however, subject to exceptions. Many cases are observed in which pigmented stripes are first observed on finger-nails other than the first and in which the regular sequence of pigmentation is not followed.

There is also a tendency for the pigmentation to be symmetrically bilateral, appearing on the same nails of both hands. This also is not true in every case.

IS THE PIGMENTATION NEVOID IN CHARACTER?

In view of the fact that pigmented stripes occur so regularly in Negroes and follow definite rules as to their occurrence, one is led to the conclusion that they are not nevoid in character, but are manifestations of a normal physiologic process. The stripes must be due to an increased pigment-producing capacity in the corresponding portion of the nail matrix.

SUMMARY AND CONCLUSIONS

1. Pigmentation of the nails in the Negro is a normal finding of common occurrence.

2. It takes the form usually of pigmented longitudinal stripes. In the darker Negroes there may be in addition a diffuse pigmentation of the nail substance.

3. The pigment particles are found scattered through the nail cells, more especially the deeper layers and are more concentrated in the areas corresponding to the stripes. The pigment is undoubtedly melanin.

4. Pigmented stripes may appear at any age, but are not usually present at birth.

5. There is a progressive increase in their occurrence with increasing age.

6. There is a tendency for more of the nails to be involved with increasing age.

7. In the lighter Negroes such pigmentation is uncommon. With increased skin pigmentation, there is a definitely increased nail pigmentation.

8. There are no differences in nail pigmentation between the two sexes.

853 Seventh Avenue.

POIKILODERMA ATROPHICANS VASCULARE, JACOBI

REPORT OF A CASE WITH A REVIEW OF RECENT LITERATURE

LAURENCE TAUSSIG, M.D.
SAN FRANCISCO

The symptom complex that was first designated poikiloderma atrophicans vasculare by Jacobi in 1907 [1] is an unusual condition. A number of cases have been presented at various dermatological meetings in this country and in Europe. In nearly every instance a controversy developed as to whether the condition was entitled to a special classification or whether it was simply an unusual form of one of the more common skin conditions. The rarity of the disease and its controversial status induced me to report a typical and well developed case. The patient was shown at the meeting of the San Francisco Dermatological Society on Oct. 10, 1930, and the diagnosis was concurred in by those present.

REPORT OF A CASE

History.—D. McG., a boatman, aged 53, entered the Marine Hospital at San Francisco for treatment for an ulcerated area that had developed on the inner surface of his left arm three months previously. He was referred to the University of California outpatient department for the diagnosis of an associated generalized eruption. This eruption had been present for twenty years, first involving the inner and anterior surface of the left thigh and gradually spreading over the thighs and arms and later to the body, legs, forearms and recently to the face. There had been no subjective symptoms except a moderate loss of muscular strength during the past four years. The ulcerated area was exquisitely sensitive and incapacitated the patient for his usual occupation. Almost the entire surface of the skin was involved, islands of normal skin occurring on the buttocks, the back, the abdomen and the penis. The face and hands were for the most part normal, and the scalp was entirely free from lesions.

Examination.—The eruption was moderately scaly in practically all regions, and consisted of pigmented areas, telangiectatic macules and atrophic depigmented spots. These were arranged in a blotchy, bizarre manner. The individual lesions varied in size from that of a coin to palm-sized and larger. The first impression was

---

Submitted for publication, June 29, 1931.

From the Division of Dermatology, University of California Medical School.

1. Jacobi, E.: Fall für Diagnose (Poikilodermia atrophicans vascularis), Verhandl. d. deutsch. dermat Gesellsch., IX Kongress, Bern, 1906, **9**:321, 1907.

of a chronic roentgen dermatitis in some locations, while in others a premycotic mycosis fungoides was suggested. In other situations, especially the forearms and face, the eruption simulated a fixed phenolphthalein rash.

The skin of the back was diffusely scaly and crenated, with a few small islands of normal skin over the left shoulder and between the scapulae. The lesions varied in color from dark brown to livid or rose red, with varying degrees of telangiectasia. There was mottling of depigmented spots giving a reticulate appearance.

The chest and abdomen were mottled with erythematous and depigmented atrophic areas. The skin was wrinkled, especially over the left mamma. The

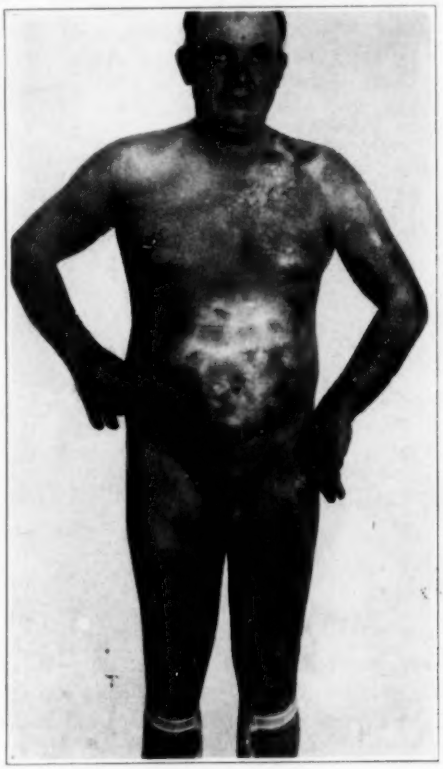

Fig. 1.—Anterior view of the patient.

abdomen presented depigmented spots and coin-sized and larger erythematous, brown and livid spots. Telangiectases were scattered over the anterior surface of the trunk, notably over the upper part of the abdomen.

The thighs were practically covered with scaly, wrinkled, atrophic skin which was deep red. There were a number of soft nodules scattered over the anterior surface of the left thigh. Most of the pubic hair was absent. The penis was free from the eruption, but the scrotum was the site of reticulated pigmentary changes. There was an irregular area of normal skin around the intergluteal fold. The legs presented some atrophic changes, but the feet were clear.

On the arms were rather large crenated patches. On the inner surface of the left arm was a circular ulcer, 6 cm. in diameter, not excavated or indurated, but very sensitive to the slightest touch. The muscles of the left shoulder and arm were atrophied, probably from disuse. The forearms presented a few coin-sized patches of telangiectasia and pigmentation. The axillae and hands were free.

The scalp presented two coin-sized areas with keratotic follicular plugs. A few small nummular erythematous and scaly patches were present on the forehead, and there was a diffuse scaly area on the chin. The upper lids were slightly reddened and thickened.

The mucous membrane of the mouth was not involved.

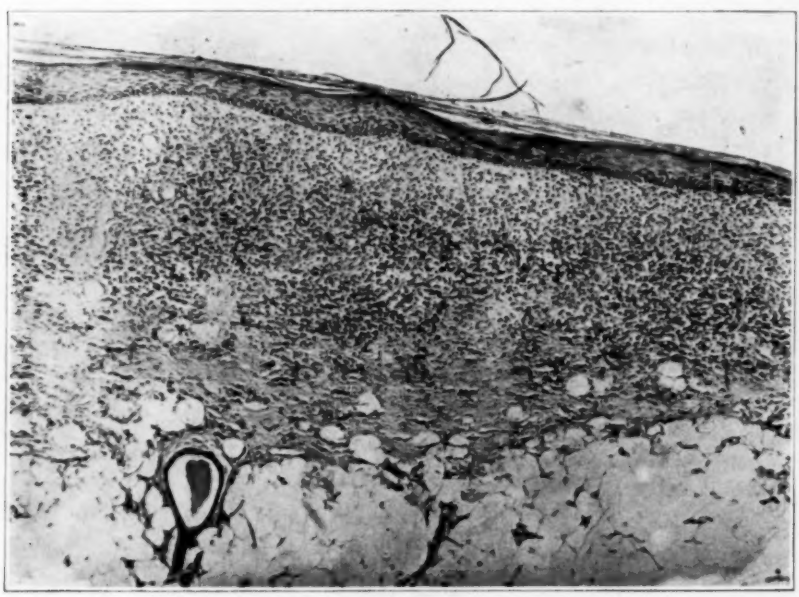

Fig. 2.—Low power photomicrograph of a section from the anterior part of the left thigh, showing the actively growing mesenchymal endothelial tissue separating the epidermis from the corium. The degenerative remainder of a hair follicle is visible in the lower left corner.

Physical examination revealed no remarkable abnormalities, and the laboratory tests showed no deviation from the normal.

Course.—During the course of a few months, the ulcerated lesion on the arm healed under the influence of bland ointments, leaving a moderately thickened scar. The skin condition in general showed no noticeable change.

The patient returned for observation six months later, and at that time a dozen or more soft nodules similar to those noted on the left thigh at the first examination were to be seen on the right side of the chest and abdomen. The patient's health had remained good, though an occasional superficial excoriation had appeared from time to time on the scar on the arm.

Histologic Findings.—Two specimens of tissue were removed for microscopic study. One was from the anterior surface of the left thigh, an apparently active, soft nodule being chosen. This was clinically the early phase of the eruption in contradistinction to the second specimen, which was taken from what appeared to be the end-result of the process. The second specimen was taken from the lower portion of the back on the left side. The skin in this region was slightly scaly and thin, with moderate crenation. There were telangiectases and mottled pigmentation and depigmentation.

The histologic report was written in collaboration with Dr. C. L. Connor, Professor of Pathology at the University of California Medical School. Sections of the material from the thigh showed a fairly sharply limited layer just beneath

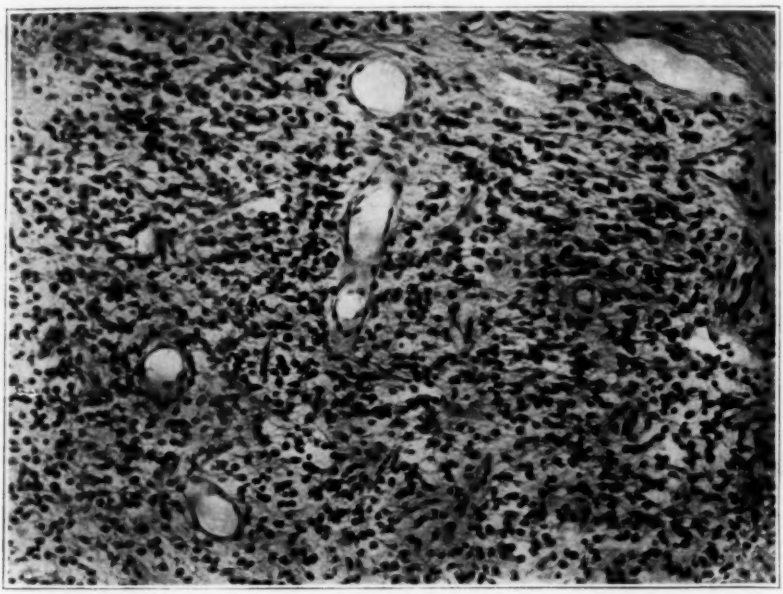

Fig. 3.—Higher power photograph of figure 2, showing the active development of new blood vessels and the endothelial character of the newly developed layer.

the epidermis, apparently separating this structure from the corium. This layer consisted of growing mesenchymal tissue, made up for the most part of endothelial cells forming capillaries and fibroblasts. Some of the capillaries contained blood. This newly formed structure had the appearance of embryonal mesenchyme, and was not characteristic of granulation tissue or of true tumor. The epidermis was flattened out, obliterating the rete pegs and consisting of from 8 to 10 somewhat compressed cells. Vacuolization of the cells occurred here and there in the epidermis. The basal layer was destroyed, and in some places the fibroblasts of the newly formed layer and the epithelial cells were so intermingled that they could not be differentiated from one another. No pigment-containing cells were seen. In the infiltrating layer there were no sweat glands, sebaceous glands or hair

follicles, but the remains of hair follicles were to be seen in the underlying corium. There were also some endothelial new growth in this region and an endothelial proliferation between fat cells. Occasional eosinophilic granulocytes and polyblasts were present in the section.

Sections of the specimen from the lower part of the back were essentially similar to those from the first specimen, except that the process had become more mature. There was condensation of the tissue, with a greater amount of intercellular substance. The capillaries had collapsed and were represented by double rows of endothelial cells or by small clumps of cells. The myxomatous appearance of embryonal connective tissue was still somewhat apparent. The epidermis was still further thinned out, consisting of from four to six layers of flattened prickle cells. The basal layer was absent, but the demarcation between the epidermis and the infiltrating layer was sharper than in the first section. In some places there were groups of stellate melanoblasts at the basal edge of the epidermis, and in the endothelial layer were pigment-containing phagocytic cells, probably containing melanin from broken-down melanoblasts. In the deep layers there was also some blood pigment. There were fewer polyblasts and eosinophils in this section. The connective tissue of the corium was hyaline, comparatively acellular and contained few blood vessels. Remnants of sweat glands were buried deeply in this layer.

The special stains added little to the histologic picture. There was abundant elastic tissue in the corium beneath the layer of tissue reaction, but, as would be expected, there was none in the newly formed tissue. Medullated nerve fibers were present as usual in the corium, but these were interrupted by the layer between the corium and the epithelium.

Histologically, the process consisted in the development of a layer of growing tissue interposed between the normal corium and the epidermis. In the course of this process the epidermis was flattened out, and the corium showed hyaline degeneration. There was nothing present in the sections to account for this peculiar reaction. It more nearly resembled a slow-growing mesenchymal tumor, not encapsulated, yet definitely nonmalignant. Mitotic figures could be found, but they were very rare.

COMMENT

Lane[2] published the first article in the American literature on poikiloderma in 1921, and supplemented this with a second article in 1923.[3] He reviewed the literature on the subject and the cases reported up to that time. Since then, a considerable number of cases have been presented at dermatologic meetings both here and abroad, and a number of articles have appeared in the literature. Most of the authors have tentatively considered the condition a disease *sui generis*. A tendency has developed to divide poikiloderma into several groups.

---

2. Lane, John E.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **4**:563 (Nov.) 1921.

3. Lane, John E.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **8**:373 (Sept.) 1923.

The following is the classification suggested by Petges,[4] to which a fourth group has been added.

1. Poikiloderma of Civatte.
2. Poikiloderma atrophicans vasculare (Jacobi).
3. Poikilodermatomyositis (Petges-Cléjat).
4. Scleropoikiloderma.

In 1923 Civatte [5] published an account of three patients, the case of one having previously been reported as an example of "poikiloderma of Petges-Jacobi." The patients were women at or past the menopause. The eruption consisted of a reticular pigmentation limited to the face, neck, upper part of the chest and arms. In the two cases that were observed over a considerable period, the eruption cleared entirely under the administration of suprarenal extract. Civatte considered that the eruption was due to a glandular dysfunction associated with the menopause, and decided that though there was a superficial resemblance to the generalized types of poikiloderma, it was a different disease. A number of cases have been reported in the French and English literature that correspond closely to this group.

Jacobi, in 1907 [1] and again in 1906,[6] published the description of a patient he had presented at the ninth congress of the German Dermatological Society in Bern in 1906. This report has been the model for most of the cases subsequently described under the term poikiloderma. The condition was characterized by telangiectasia, hyperpigmentation, depigmentation and atrophy, all forming a marmoraceous network over most of the skin area. The development was gradual, covering a period of years, with relatively slight subjective symptoms, which consisted of loss of muscular power and moderate pruritus. A rather large number of cases have been reported that correspond closely to Jacobi's.

In a number of cases reported in the French literature the patients have presented an eruption quite similar to that of the Jacobi group, but differing by the association of a marked myositis and muscular atrophy. The model for this group is the patient reported by Petges and Cléjat,[7] in 1906, under the title of "Sclérose atrophique de la peau

4. Petges, G., and Petges, A.: Poïkilodermatomyosite dans la jeunesse et l'enfance, Ann. de dermat. et syph. **1**:441, 1930.

5. Civatte, A.: Poikilodermie reticulée pigmentaire du visage et du cou, Ann. de dermat. et syph. **4**:605, 1923.

6. Jacobi, E.: Poikilodermia atrophicans vascularis, Ikonographia Dermatologica, 1908, no. 3, p. 95.

7. Petges and Cléjat: Sclérose atrophique de la peau et myosite généralisée, Ann. de dermat. et syph. **7**:550, 1906.

et myosite généralisée." Petges and his associates in recent articles have designated this group under the title of poikilodermatomyositis. It is noteworthy that muscular weakness is a frequent concomitant of the poikiloderma of Jacobi, and it is probable that this variant is one of degree rather than of kind.

Rottmann [8] and Jaffé [9] have reported instances in which a typical poikiloderma of the generalized type was associated with a marked sclerodactylia. Jaffé called this group scleropoikiloderma, and he did not consider poikiloderma a disease entity. Jadassohn, in discussing the case presented by Jacobi and certain cases presented subsequently by others, considered the disease as a probable variant of scleroderma. The occurrence of these cases associated with sclerodactylia strengthens this point of view.

The variations described indicate the difficulty that arises in deciding whether a disease entity is being dealt with or whether the condition is merely a symptom of one or several underlying diseases. It seems reasonable to agree with Civatte in excluding the localized eruption that he described from the generalized types.

DIFFERENTIAL DIAGNOSIS

As Wise noted in discussing the presentation of Lane,[2] a typical case of poikiloderma atrophicans vasculare resembles no other eruption. The conditions that have been frequently considered in the differential diagnosis are: lupus erythematosus, scleroderma, Majocchi's disease, angioma serpiginosum, acrodermatitis chronica atrophicans and roentgen dermatitis. None of these conditions is simulated by a well developed case of poikiloderma, though some of the features of each may be present to a striking degree.

Lupus erythematosus of the disseminated type differs markedly in its clinical appearance and course. Atrophic changes subsequent to this condition are circumscribed, and there is a definite tendency toward localization. It is not conceivable that a toxic eruption such as lupus erythematosus could be as extensive in its distribution as poikiloderma without marked general symptoms.

With the exception of the cases that are associated with sclerodactylia, the connection between poikiloderma and scleroderma is very slight. In poikiloderma there is an apparently inflammatory stage such as may occur in scleroderma, but there is never a thickening of the skin

8. Rottmann, H. G.: Ueber Poikilodermia atrophicans vascularis (Jacobi) mit bemerkenswerter Nebenbefunden, Arch. f. Dermat. u. Syph. **153**:747, 1927.

9. Jaffé, Kaete: Zwei Fälle von Sklero-Poikilodermie, Arch. f. Dermat. u. Syph. **159**:257, 1930.

to palpation, and the lesions do not occur in localized plaques. Furthermore, the histologic picture does not show the fibrotic changes typical of scleroderma.

Purpura annularis telangiectodes is usually limited to the lower extremities and is characterized by the shape of the lesions and the tendency of the individual lesions to clear, leaving pigmentation. The pathologic findings in Majocchi's disease are characteristic.

In angioma serpiginosum the eruption is rarely generalized, and the individual lesions are primarily angiomatous, extending peripherally and presenting satellite spots. The degree of atrophy is usually very slight.

Clinically, the resemblance of poikiloderma to acrodermatitis chronica atrophicans is closer than to any other condition. It differs in that acrodermatitis is limited to the limbs, as a rule, and usually to the distal portions. Both conditions present a preliminary inflammatory stage followed by atrophy. Acrodermatitis does not develop a mottled appearance, and lacks the bizarre configuration of poikiloderma.

The marked similarity to roentgen dermatitis is frequently mentioned, and at first glance is striking. However, on close examination, the resemblance is seen to be superficial. The typical sharp borders marking the limits of the radiated fields are absent; there is no tendency toward the development of keratoses or degenerating foci, and the history of exposure to the rays is lacking.

The cases reported in which there was a fatal termination with necropsy have not cast any light on the possible cause of the skin changes, and the causes of death were evidently coincidental.

STATISTICAL REVIEW OF THE LITERATURE

It is difficult to decide from the descriptions published in society transactions whether a given case should properly be classed with the poikilodermas or not. The literature since the publication of Lane's second article in 1923 has been reviewed, and the cases in which the condition was called poikiloderma atrophicans vasculare and those that seemed to belong to this classification have been listed in the accompanying table, with the age and sex of the patient, the duration of the disease and any special feature of the particular case. The cases that were evidently examples of the Civatte type have been excluded in agreement with Civatte's opinion that they properly belong in a separate category. The total number of cases listed is sixty-four. Thirty-seven of these were in women and twenty-three in men; in the remaining four cases the sex was not stated in the available report or abstract. The youngest patient was 6 years and the oldest 78 years of age, with an average of 35 years. The duration of the disease varied from three months to thirty-eight years.

Cases of Poikiloderma Atrophicans Vasculare, Exclusive of Those of the Civatte Type, Appearing in the Literature Since 1923

	Author	Age	Sex*	Duration	Comment
1.	Wile: Arch. Dermat. & Syph. **8**: 864 (Dec.) 1923	43	♀	27 yr.	None of the discussers agreed with the diagnosis
2.	Klauder: Arch. Dermat. & Syph. **10**: 639 (Nov.) 1924	31	♀	5 yr.	Improvement under treatment with suprarenal extract, pills of ferrous carbonate, U. S. P., and arsenious acid
3.	Hollander: Arch. Dermat. & Syph. **10**: 644 (Nov.) 1924	33	♀	12 yr.	Colored woman
4.	Whitehouse: Arch. Dermat. & Syph. **10**: 651 (Nov.) 1924	13	♀	?	Followed an arsenic dermatitis
5.	Oppenheim: Zentralbl. f. Haut-u. Geschlechtskr. **9**: 443, 1923-1924	34	♀	3 mo.	Histology compatible, but no thinning of the skin
6.	Bruck: Zentralbl. f. Haut-u. Geschlechtskr. **13**: 24, 1924	54	♀	14 yr.	
7.	Fritzsche: Zentralbl. f. Haut-u. Geschlechtskr. **14**: 27, 1924	75	♂	10 yr.	Werther disagreed with the diagnosis, calling the condition pityriasis lichenoides chronica
8.	Dohi: Japan. J. Dermat. & Urol. **24**: 24, 1924	6	♀	2½ yr.	Associated with marked muscular atrophy
9.	Naegeli: Zentralbl. f. Haut-u. Geschlechtskr. **15**: 35, 1924	9	♀	?	Started at birth
10.	Bernhardt: Przegl. dermat. **19**: 103, 1925	?	?	?	
11.	Rosenberg: Zentralbl. f. Haut-u. Geschlechtskr. **16**: 887, 1925	?	?	?	
12.	Schmidt: Zentralbl. f. Haut-u. Geschlechtskr. **17**: 45, 1925	?	?	6 yr.	Associated with sclerodactylia-like changes
13.	Volk: Zentralbl. f. Haut-u. Geschlechtskr. **17**: 416, 1925	?	?	2 yr.	
14.	Rasch: Brit. J. Dermat. **37**: 477, 1925	61	♂	38 yr.	Leukoplakia of the hard palate and an associated carcinoma of the stomach
15.	Wertheim: Arch. f. Dermat. u. Syph. **151**: 396, 1926	67	♂	20 yr.	Atrophy of the hypophysis found at necropsy; died of carcinoma of the pancreas
16.	Williams: Arch. Dermat. & Syph. **13**: 694 (May) 1926	16	♀	8 yr.	
17.	MacKee and Wise: Arch. Dermat. & Syph. **13**: 703 (May) 1926	17	♂	10 yr.	Lane considered the condition Majocchi's disease
18.	Wolf: Arch. Dermat. & Syph. **13**: 716 (May) 1926	17	♀	9 wk.	Doubtful case
19.	Wertheimer: Arch. Dermat. & Syph. **14**: 594 (Nov.) 1926	43	♂	7 yr.	
20.	Crawford: Arch. Dermat. & Syph. **14**: 594 (Nov.) 1926	32	♂	2 yr.	
21.	Mierzecki: Arch. f. Dermat. u. Syph. **152**: 751, 1926	43	♂	25 yr.	Died of sepsis secondary to multiple ulcers
22.	Fuhs: Dermat. Ztschr. **48**: 34, 1926	6	♀	?	
23.	Bloch: Schweiz. med. Wchnschr. **56**: 753, 1926	24	♀	5 yr.	Associated with internal gland dysfunction
24.	Leszczynski: Zentralbl. f. Haut-u. Geschlechtskr. **22**: 627, 1927	35	♂	10 yr.	Associated with dysfunction of the hypophysis
25.	Geisler: Dermat. Wchnschr. **85**: 1133, 1927	50	♂	?	
26.	Wohlstein: Therapia (Bratislava) **6**: 4, 1927	35	♀	?	
27.	Rottmann: Arch. f. Dermat. u. Syph. **153**: 747, 1927	58	♂	8 yr.	Associated with sclerodactylia and cutaneous calcinosis
28.	Bowman and Clark: Arch. Dermat. & Syph. **15**: 583 (May) 1927	39	♂	16 yr.	A case of mental disease: autopsy failed to give a clue to the etiology of the skin condition
29.	Traub: Arch. Dermat. & Syph. **15**: 728 (June) 1927	16	♀	8 yr.	
30.	Adrian: Bull. Soc. franç. de dermat. et syph. **32**: 114, 1925	31	♀	7 yr.	
31.	Ulitzka: Dermat. Ztschr. **54**: 119, 1928	24	♀	4 yr.	Associated with marked muscular atrophy over the thorax and arms
32.	Wile: Arch. Dermat. & Syph. **18**: 480 (Sept.) 1928	66	♀	2 yr.	
33.	Tulipan: Arch. Dermat. & Syph. **18**: 924 (Dec.) 1928	44	♀	22 yr.	
34.	Oliver and Finnerud: Arch. Dermat. & Syph. **17**: 435 (March) 1928; **18**: 971 (Dec.) 1928	8	♀	3 yr.	Bloch considered that this would be a typical case of poikiloderma in the course of ten years
35.	Liebner: Zentralbl. f. Haut-u. Geschlechtskr. **27**: 746, 1928	61	♀	24 yr.	
36.	Chalipskij: Russk. Vestnik. Dermat. **6**: 564, 1928	29	♂	20 yr.	

* In this table ♀ indicates female; ♂, male.

Cases of Poikiloderma Atrophicans Vasculare, Exclusive of Those of the Civatte Type, Appearing in the Literature Since 1923—Continued

	Author	Age	Sex*	Duration	Comment
37.	Sellei: Zentralbl. f. Haut-u. Geschlechtskr. **28**: 657, 1928	45	♀	19 yr.	
38.	Pintér: Zentralbl. f. Haut-u. Geschlechtskr. **29**: 255, 1929	30	♀	4 yr.	
39.	Foldvári: Zentralbl. f. Haut-u. Geschlechtskr. **30**: 20, 1929	78	♀	38 yr.	
40.	Lutz: Zentralbl. f. Haut-u. Geschlechtskr. **30**: 451, 1929	6	♀	6 yr.	
41.	Pintér: Zentralbl. f. Haut-u. Geschlechtskr. **31**: 160, 1929	33	♂	5 yr.	
42.	Dore: Brit. J. Dermat. **41**: 122, 1929	43	♀	20 yr.	
43.	Alexander: Zentralbl. f. Haut-u. Geschlechtskr. **31**: 282, 1929	66	♀	2 yr.	
44.	Nicolau: Bull. Soc. franç. de dermat. et syph. **36**: 823, 1929	16	♀	3 yr.	Associated with muscular atrophy
45.	Jordan: Dermat. Wchnschr. **89**: 1827, 1929	18	♀	8 yr.	
46.	Jordan: ibid.....	50	♂	?	
47.	Gate, Bosonnet and Michel: Bull. Soc. franç. de dermat. et syph. **36**: 322, 1929; **36**: 839, 1929	38	♂	11 yr.	Associated with complete alopecia of the eyebrows and partial loss of the moustache and occipital hair. Later second reference), lesions clinically suggestive of mycosis fungoides developed
48.	Gougerot and Burnier: Bull. Soc. franç. de dermat. et syph. **36**: 71, 1929	34	♂	16 yr.	
49.	Petges et al.: Bull. Soc. franç de dermat. et syph. **36**: 817, 1929	31	♂	?	Associated with marked myositis
50.	Jamieson: Arch. Dermat. & Syph. **19**: 335 (Feb.) 1929	62	♀	4 yr.	
51.	Abramowitz: Arch. Dermat. & Syph. **19**: 479 (March) 1929	30	♂	7 yr.	Lane hesitated to accept this and the following case as true poikilodermas
52.	Abramowitz: ibid.....	30	♂	10 yr.	
53.	La Rocco and Cummer: Arch. Dermat. & Syph. **20**: 142 (July) 1929	35	♀	7 yr.	History of previous roentgen therapy, but no loss of hair
54.	Wile: Arch. Dermat. & Syph. **20**: 540 (Oct.) 1929	66	♀	2 yr.	
55.	Gross: Arch. Dermat. & Syph. **21**: 480 (March) 1930	28	♀	7 yr.	Clinical evidence of pituitary and thyroid changes
56.	Richter: Dermat. Ztschr. **59**: 233, 1930	52	♀	6 yr.	
57.	Jaffé: Arch. f. Dermat. u. Syph. **159**: 257, 1930	49	♀	2 yr.	This and the succeeding patient had an associated sclerodactylia
58.	Jaffé: ibid.....	60	♀	8 yr.	
59.	Geiger and Konrad: Arch. f. Dermat. u. Syph. **159**: 1, 1930	46	♂	14 yr.	
60.	Geiger and Konrad: ibid.....	32	♀	16 yr.	
61.	Petges and Petges: Ann. de dermat. **1**: 441, 1930	18	♀	1¼ yr.	Associated with marked muscular atrophy; patient died of pulmonary tuberculosis
62.	Petges and Petges: ibid.....	7½	♂	3 yr.	Marked loss of strength; probably congenitally syphilitic
63.	Oulmann: Arch. Dermat. & Syph. **23**: 363 (Feb.) 1931	40	♂	12 yr.	
64.	Schwartz: Arch. Dermat. & Syph. **23**: 783 (April) 1931	40	♂	4 mo.	Intracellular and extracellular diplococci were seen in the biopsy sections

* In this table ♀ indicates female; ♂, male.

CONCLUSIONS

1. A well developed case of poikiloderma atrophicans vasculare of the Jacobi type is described.

2. The histologic findings suggest a slow-growing mesenchymal tumor-like process rather than an inflammatory reaction.

3. The condition should be considered a disease *sui generis* on the basis of its histology as well as on that of its clinical appearance.

ABSTRACT OF DISCUSSION

Dr. Harold N. Cole, Cleveland: I think the disease poikiloderma is so rare that every case should receive careful study. Only in that way can we arrive at a definite understanding of it. I agree with Dr. Taussig that the Civatte type should not be included, and I consider it a separate entity.

Dr. Marion B. Sulzberger, New York: I want to talk less about the morphology of this disorder than about the question as to whether poikiloderma is always one and the same condition. I believe it is a clinical entity, but I believe it corresponds very much to the other atrophies, in that we must distinguish between the idiopathic and the secondary types. When we say "idiopathic," we must realize that this means only that we do not know the cause or do not see any manifest reason for the change in the skin. There must have been a cause, only our present methods do not enable us to detect it. Some of these cases are associated with scleroderma, as Dr. Taussig brought out, and there are also atrophies and other types of disorder associated with poikiloderma. Then there are the cases of the type Civatte described, and those associated with, if not caused by, endocrinologic pathologic processes. This association is also usually true of the Civatte type of poikiloderma. If you read Dr. Taussig's paper in extenso, you will see that many of the poikilodermas have some change in the hypophysis. I think many syndromes should be preserved as clinical entities, and we should still realize that in this way we are bringing under one head a multitude of conditions with many different causes. We know that clinically and histologically identical skin lesions can be due to different agents. The best examples of this are lichen planus and herpes zoster. For instance, an eruption can be absolutely indistinguishable from a true (idiopathic) lichen planus and still be due to arsenic.

Until we are sure of etiologies, we must bear in mind that our clinical and morphologic entities are not necessarily, and in fact probably are not, etiologic units. This applies to poikiloderma as well as to cancer or to psoriasis or to any other lesion of unknown cause.

Dr. Ludwig Oulmann, New York: Some of you may remember that in the last number of the Archives there was an article on poikiloderma. The cases reported, like this of Dr. Taussig's, showed an endocrine alopecia areata, which might bring up the relationship of the endocrine feature. There was an etiologic feature in which the epidermis was raised entirely, and the patient had great masses of lesions. The case was interesting from another standpoint, in that the patient was in a military camp in 1918, and we know from the German literature that exposure to cold and weather plays a great rôle in the development of poikiloderma.

Dr. Laurence R. Taussig, San Francisco: In going over the case histories in the literature, it was interesting to find that in many endocrine gland dyscrasia was mentioned. It is difficult to evaluate the part internal gland dyscrasias play, and it will take some time to determine this point. It is interesting to note that the incidence of cancer is extremely high in the fatal cases that have been reported. One case of cancer of the pancreas, one of cancer of the stomach and another in which I do not recall the location of the cancer have been reported.

SPONTANEOUS SPIROCHETOSIS AND EXPERIMENTAL SYPHILIS IN RABBITS

S. M. FRIED, M.D.
AND
S. S. ORLOV, M.D.
MOSCOW, U. S. S. R.

The morphologic identity of Spirochaeta pallida and Spirochaeta cuniculi and the resemblance between the processes caused by these micro-organisms, respectively, in the animal body cast a shadow of doubt, at the very beginning, on the value of the results obtained from the study of experimental syphilis in the rabbit. More than that, they have led Arzt and Kerl, Klarendon and Simon and others to the belief that the existence of a spontaneous spirochetosis in the rabbit makes this animal altogether useless for the study of experimental syphilis. However, the majority of investigators (Jacobstahl, Kolle, Mulzer, Uhlenhuth and others), basing their results on comparative studies of spontaneous spirochetosis and of experimental syphilis, have expressed the opinion that in spite of the morphologic resemblances of both strains, the contrast of the diseases that they cause respectively is rather sharp, and the margin of error in their discrimination is practically nil.

In this article we shall present the comparative characteristic traits of these two infections in the rabbit and also the fundamental differential signs that will enable one to make a correct diagnosis of these infections.

The results obtained are based not only on the study of literature but mainly on personal observations during an epidemic of spirochetosis, and also on a six years' investigation of experimental syphilis in over 1,000 rabbits.

From February, 1927, to March, 1928, we had the opportunity in Moscow to study two epidemics of spontaneous spirochetosis which in their dimensions exceeded any hitherto described in the literature. The history of the onset and the course of these epidemics are briefly as follows:

Early in the fall of 1926 the managers of one large farm discovered in about 100 rabbits anogenital lesions of a peculiar character. Because of ignorance on the part of those in charge of the animals, the rabbits were not isolated, and by February, 1927, 640 (16.1 per cent) of 5,000

Submitted for publication, June 9, 1931.
From the State Venereologic Institute, named after Professor Bronner.
This article was translated from the Russian by Dr. B. M. Fried, Boston.

were ill with spontaneous spirochetosis. Energetic treatment with bismuth and arsphenamine was then undertaken, and apparently controlled the epidemic. However, eight months later, when the number of animals in this farm had reached 12,000, a new epidemic was discovered. This probably resulted from the fact that the apparently healthy animals were not examined by us on our first visit, and no prophylactic treatment was given. This time, 704 (19.3 per cent) of 3,650 rabbits showed this spontaneous disease.

All rabbits found on the farm showed a susceptibility to infection with the micro-organism of spontaneous spirochetosis. It occurred more frequently in females at the age of 1 year (54.9 per cent) than in males of the same age (34.9 per cent). In general, age seemed to play a particular rôle in the infection: Thus, of 2,893 animals which were 1 year of age and above and which had been mated there were 1,304, or 46.4 per cent, affected with this condition, whereas of 5,800 rabbits whose age did not exceed 8 months and most of which were not yet mated there were only 40, or 0.7 per cent, diseased. This would be in favor of the theory that the common means of spreading the infection among rabbits is genitally, by way of sexual intercourse or merely by genital contact. Extragenital transmission of the disease should be regarded as nonessential. It is hardly possible to speak of the occurrence of a "legitimate" percentage of this condition on a given farm. In reality, the spread of the illness is wholly connected with the zootechnical and hygienic condition in which the animals live.

Spirochaeta cuniculi by its morphology is identical, or very nearly identical, with Spirochaeta pallida, although some authors have stressed differences between the two micro-organisms when stained with the Warthin-Stairy method and when examined under dark-field illumination. However, the differences are so insignificant and, judging from the descriptions given, so contradictory that they cannot serve as a basis for differentiation. The culturing of Spirochaeta cuniculi on artificial mediums has, as is known, failed up to the present time.

Both diseases have nearly the same incubation period: from two and a half to three and a half weeks in syphilis and from three to four weeks in spirochetosis. However, deviations from this term were occasionally observed: from five to eleven, fourteen, seventy-two, eighty-three and one hundred and eighty-three days, according to Adachi, Frei, Klarenbeck, Kolle, Noguchi, Schereschewsky and Worms. The prolongation of the incubation period was observed in instances of natural genital infection, and in experimental syphilis it varied from seven and ten days to three, four, six and even ten months (Brown and Pearce, Frei, Uhlenhuth and Mulzer, Kuczynski, Finkelstein, Orlov, Ezersky).

THE CLINICAL PICTURE

From the clinical standpoint spontaneous spirochetosis of the rabbit represents first, and in most instances only, disease of the external genitalia, often accompanied by perianal lesions. In fact, we have never found an animal with this condition in which the anogenital area was spared.

The process ordinarily starts with hyperemia and edema of the prepuce in the male (fig. 1) and of the labia majora in the female. In the latter there occurs a spontaneous mucopurulent secretion from the deeper parts of the vulva and even from the vaginal mucosa, containing spirochetes. The anal lesions are detected on superficial inspection, but quite often slight hyperemia, edema and superficial erosions are found in the depth of the rectum about 0.5 or 0.75 cm. from the external sphincter. As time goes on, the edema increases in intensity and the inflamed areas appear as bluish-red spots at the edges of the prepuce or labia majora

Fig. 1.—Spontaneous spirochetosis. An early lesion of the prepuce.

where small hemorrhagic spots are also found, the removal of which discloses bleeding erosions. The anal lesions develop in a similar way. Sometimes the early lesion has a more circumscribed character, showing in the area of the genitalia small erosions covered with crusts and a very mild inflammatory reaction. The disease has a definite tendency to spread at the periphery, gradually invading the hairy parts. However, it never invades the skin of the belly or that of the tail, always remaining within the anogenital boundaries. When observed in the hairy parts, the lesion is somewhat different, being much milder in character. The inflammatory reaction is less pronounced, and the process is seen as pale yellow or yellowish-gray verrucose overgrowths having a rosette-like appearance with a central inflammatory zone. In rare instances, when the intensive inflammatory process invades the hairy part of the skin the entire anogenital region shows a diffuse marked edema, the genital organs being barely visible; this leads in the male to phimosis and in the female to obliteration of the vaginal orifice, which is covered with thick

dark brown crusts. After removal of the crusts there appears an eroded and, in places, bleeding surface, resembling a humid syphilitic condyloma. It is of importance to note that in no instance could an induration be observed. As was noted by Kolle, Ruppert and Möbius, the lesions are undoubtedly quite painful.

Contrary to what one sees in spontaneous spirochetosis, the syphilitic chancre in the rabbit (fig. 2 *A*) presents in most instances a marked induration invading the entire thickness of the skin, and when confined to the testicle it is accompanied by a periorchitis (fig. 2 *B*). Very frequently there occurs a deep central necrosis. There is practically no inflammation at the periphery. However, we must admit that when the hard chancre is confined to the vulva or the prepuce it lacks the typical

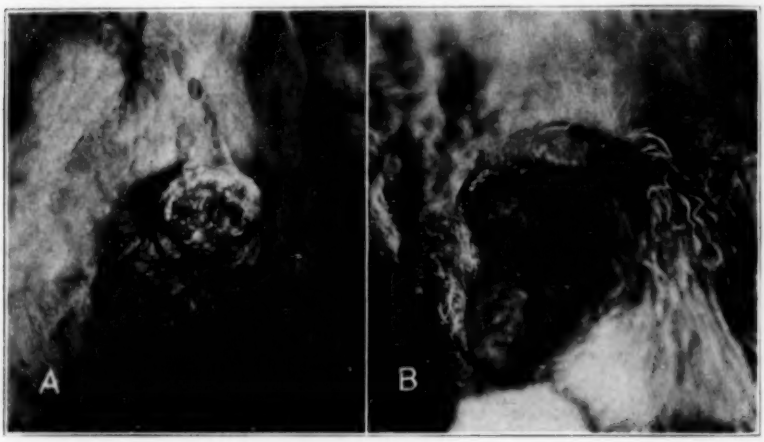

Fig. 2.—*A*, syphilitic chancre in the rabbit. *B*, syphilitic periorchitis in the rabbit.

traits just described, showing merely one or two small infiltrated erosions, with or without induration. But even in these instances the chancres can be differentiated from early spontaneous spirochetosis by their sharp boundaries, the absence of inflammation around the lesion and the presence of a mucopurulent discharge from the vulva.

Foci of spontaneous spirochetosis may simultaneously occur in other places of the rabbit's skin than the anogenital region. Frei, Klarenbeck, Ross, Ruppert, Schereschewsky, Kandiba, Retchmensky and Pavlov have described such lesions, which Frei and Ruppert regarded as the result of the generalization of the micro-organism; by analogy with syphilis, the lesions were classified into primary and secondary. Schereschewsky and Worms have regarded them as the product of superinfection.

It is true that the "dissemination" of the germ is not of rare occurrence. Thus it was found in 198, or 14.7 per cent, of 1,344 rabbits. The favored localization of this disease is near or around the mucosa, principally around the mouth, the lower lip and the chin (112, or 8.3 per cent of the cases), then on the upper lip and in the region of the moustache (fig. 3 *A*) (84, or 6.2 per cent) and less commonly in the area of the lids (41, or 3.1 per cent), and around the nose (2.5 per cent) and testicle (3.9 per cent). Much more rarely is it found on the trunk or extremities (0.6 per cent). In a few instances the process was simultaneously localized in several places: the lower lip, the alae nasi, the upper lip, the lid (fig. 3 *B*), the testicle, etc. The body and the extremities are less often affected. In some of our rabbits the number

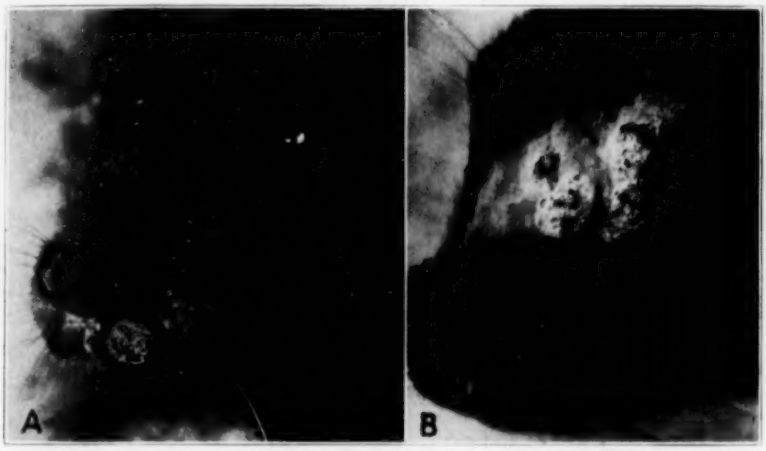

Fig. 3.—*A*, spontaneous spirochetosis. The lesion is seen on the upper lip and in the region of the moustache. *B*, spontaneous spirochetosis. A lesion in the region of the upper lid.

of foci reached fifteen. No symmetry was observed in the cutaneous lesions. The disease when localized in the skin showed no particular inflammatory changes like those seen in the genito-anal region. The cutaneous lesions appeared as papules having a tendency to spread in a verrucose manner, which has led some authors (Warthin, Buffington) to compare them with the acute condylomas seen in man. The size of the papule was usually that of a millet seed, sometimes that of a large lentil and more rarely that of a ten cent silver piece. The individual papules also had a tendency to group themselves together, to spread at the periphery and to coalesce. In the affected area the hair usually fell out. However, with the healing of the disease a new growth of hair occurred, and no trace of the lesion was left.

The pathogenesis of the multiple lesions is not yet understood. In the majority of instances they most likely represent superinfections, i. e., autosuperinfections, or else they result from primary extragenital contamination. The researches of Warthin, who found spirochetes in the blood of six rabbits with spontaneous spirochetosis, as well as those of Uhlenhuth, who was able to produce a cutaneous dissemination by intravenous and intracardiac infection of young rabbits, would be in favor of the hypothesis that, at least in some animals, the cutaneous lesion is caused by the circulating spirochete. In two of our rabbits there were so many foci that it is almost unbelievable that all of them resulted from a superinfection.

Secondary lesions in experimental syphilis, being the product of the generalization of Spirochaeta pallida, are early differentiated from those of spontaneous spirochetosis by their morphology and also, at

Fig. 4.—Syphilis localized at the border of the upper lid.

least partly, by their localization. The secondary lesions in syphilis usually appear from three to three and a half months after the infection, being confined in order of their frequency to the testicle, the edge of the lid (fig. 4), the nose, the root of the ears, the area around the anus, the skin of the forepaw and tibia and the prepuce. In instances the disease is confined to one of these places; in others it is found simultaneously in many areas, having a symmetrical distribution. In very rare cases the syphilitic lesion is found on the back or the belly, and still more rarely in the nostrils. The elements of the syphilitic disease are morphologically of the ecthymal or papulocrustaceous variety. They have a focal arrangement, are indurated and lack inflammation and central necrosis. The cutaneous lesions in spontaneous spirochetosis, then, differ from those met with in the disease caused by Spirochaeta pallida.

Primary syphilitic lesions in the rabbit are always accompanied by a regional adenopathy which is particularly evident at the acme of the

process. Swelling of the tributary lymph nodes is frequently seen with the secondary lesions and more rarely in recurrent rashes. In all instances the presence of spirochetes in these glands can be demonstrated by animal inoculation and also not infrequently by an ultramicroscopic examination. In spontaneous spirochetosis a regional adenopathy was observed in only 9.3 per cent of the rabbits studied by us. The glands in the groins are usually smaller and less firm than in syphilis, and apparently contain no micro-organisms. Arzt, Kerl and Frei are the only authors who have reported two positive results. In ten cases that we observed the result was always negative.

Contrary to what one observes in experimental syphilis, Spirochaeta cuniculi causes a parenchymatous keratitis in very rare instances. Orchitis is seen even more rarely, for none of our rabbits showed these lesions.

The duration of a syphilitic chancre in nontreated animals varies from two to four months. The secondary lesions last from three weeks to two months. Recurrences observed during the later period are usually those of parenchymatous keratitis, orchitis and, much more rarely, cutaneous lesions. The course of the lesions caused by Spirochaeta cuniculi is much longer (one year and more), having a greater tendency toward recurrences in the region of the genitalia.

The general condition of the animal is apparently not influenced by the infection with Spirochaeta cuniculi. It is interesting that in our material the rabbits that lived in cold barns (during the winter season) or in the open air developed more extensive lesions than those that lived in warm quarters.

A thorough examination of 285 young rabbits from litters of infected parents revealed that only 5 of those from 6 to 8 weeks of age showed characteristic lesions on the genitalia, on the prepuce and around the mouth, the anus (1 case), the lid and the nose. In only one animal was the disease widespread, with foci in the vulva, around the mouth, lids and nose and on the back.

We are inclined to believe that the infection occurred after the birth of the animals. Uterine transmission of experimental syphilis to the offspring could never be observed, for when the organs of the offspring born of syphilitic parents were inoculated into healthy animals, they always yielded negative results. Again, a prolonged observation of the young animals showed them to be in apparent good health and susceptible to a syphilitic infection. Positive results for congenital syphilis in the rabbit were reported by Grigoriev, Brown and Pearce and Wiman. Uhlenhuth and Mulzer, Finkelstein and Orlov obtained positive results by infecting pregnant mothers intravenously or intracardially with massive doses of Spirochaeta pallida.

Of other diseases observed on the rabbit genitalia, tuberculosis and scabies caused by Sarcoptes minor ought to be thought of in the differential diagnosis (fig. 5). Scabies, however, is diffuse, affecting sometimes the entire skin and the extremities. Likewise absent are the typical elements caused by the spirochete and also the inflammatory reactions when localized in the genitalia.

Unlike experimental syphilis, spontaneous spirochetosis becomes generalized apparently in very rare instances; only a few observers were able to demonstrate Spirochaeta cuniculi in the blood and also in the lymph nodes (Warthin, Arzt, Kerl, Frei). Attempts to produce the disease by inoculating normal animals with the liver, spleen and bone marrow of sick rabbits have invariably given negative results. A study of the visceral organs of 4 animals with disseminated spirochetosis gave us negative results.

Fig. 5.—Scabies caused by Sarcoptes minor.

PATHOLOGY

We have studied long-standing lesions from the testes, vulva, prepuce, lip and skin of the back. The inflammatory process is confined to the epidermis and to the superficial layers of the dermis. The infiltrate is usually not abundant, being mostly confined to the papillary and the subpapillary layers, and is composed of plasma cells, lymphoid cells and, sometimes, granulocytes. Occasionally fibroblasts and epithelioid-like cells can be seen. The perivascular infiltration is not constant and has no specific character. The epidermis is often thickened, showing hyperkeratosis, and at times the stratum corneum is thinned out or is altogether lacking. In places leukocytes accumulate in large numbers, forming miliary abscesses. In one instance a cloudy swelling of the epidermis and also a condition designated by French writers as "altération cavitaire" were observed. There is a verrucose prolifera-

tion of both the dermis and epidermis, and also marked hyperemia, but no particular changes are noted in the blood vessels.

Lesions found on the genitalia vary from the cutaneous lesions in that they are more pronounced, being also present in the deeper layers.

Special stains with the method of Levaditi-Manouelian and particularly with Yahnel's method as modified by Beletsky show numerous spirochetes in the epithelium and sometimes in the superficial layers of the derm. The spirochetes are particularly numerous in areas where there is thickening of the epidermis and in those places where it covers the proliferated papillae. The innumerable spirochetes are arranged in masses, sometimes occupying the entire microscopic field. Numerous spirochetes are found in the vaginal epithelium; in the superficial layers of the derm they are usually less numerous.

From the histologic point of view, the lesion represents, then, a chronic superficial inflammatory process with a tendency to a verrucose overgrowth. This is accompanied in areas by a more intense inflammation resulting in a destruction of the epithelium with the formation of erosions; the character and localization of the lesion are dermo-epidermal.

It is obvious, then, that the cutaneous lesions in spontaneous spirochetosis differ greatly from those found in syphilis. Unlike syphilis the lesion in spontaneous spirochetosis is not essentially perivascular and there are no changes in the vessel wall itself. Moreover, it is confined to the epidermis, showing verrucose proliferations that are not present in syphilis. Finally, the spirochetes are found in the superficial layers only, and the necrotic changes are much less pronounced.

To ascertain whether the visceral organs contain specific lesions we examined four rabbits with widespread cutaneous lesions. In only one did we find a miliary granuloma in the cortical layer of the suprarenal gland. A thorough search for the presence of spirochetes in this nodule gave negative results. This and the fact observed by us that granulomas of the viscera and of the brain may be observed in non-spirochetal disease in rabbits make us believe that this growth was most likely not of spirochetal origin. The question, then, of Spirochaeta cuniculi causing lesions in the viscera ought to be answered at present in the negative.

Cerebrospinal fluid was obtained from the rabbits by suboccipital puncture. The fluid of 47 animals with widely disseminated lesions of spontaneous spirochetosis was investigated. Eighteen, or 41 per cent, of this number showed an abnormal condition, such as an increase in the amount of albumin (positive Nonne and Pandi reactions) and a pleocytosis, the cells numbering from 10 to about 200 per cubic millimeter. As our supply of normal animals was limited, for economical reasons we decided to use first as controls, rabbits that

had been treated for biologic investigations with preparations of arsphenamine. Such animals ordinarily receive 0.12 or 0.15 mg. per kilogram of body weight and, following an observation period of two weeks, are kept in large cages in groups of 25 or 30 per cage. Of 76 punctured rabbits, 20 (26 per cent) yielded a pathologic cerebrospinal fluid. We then examined 59 normal rabbits, 4 of which showed a pathologic cerebrospinal fluid.

It is interesting that a pathologic study of normal rabbits that had received arsphenamine revealed lesions in the central nervous system analogous to those in rabbits with spontaneous spirochetosis. What is more, a fluid of the same kind was found in 12 per cent of normal animals. Pathologic lesions in the brains of normal animals akin to those seen in spontaneous spirochetosis were described by Iliin, Muradova, Savaneiev, Pette, Olivier (of San Francisco) and others. Professor Finkelstein of the State Venereologic Institute has found similar lesions in experimental syphilis.

The changes found in the cerebrospinal fluid of rabbits with spontaneous spirochetosis do not correspond either with the duration of the process or with its gravity. This and the fact that in no instance were spirochetes found in the cerebral foci make us believe that the changes in the fluid are not specific for spirochetosis.

The question whether rabbits with spontaneous spirochetosis are susceptible to an infection with syphilis and vice versa was investigated by us in ten animals. Five rabbits with fully developed syphilis were infected with Spirochaeta cuniculi, and five other animals with a widespread spontaneous spirochetosis were inoculated with Spirochaeta pallida. Both series of experiments yielded positive results. However, the utilization of the phenomenon of "cross-infection" for purposes of a differential diagnosis of these diseases should be guarded against. For, as was demonstrated by many observers, a rabbit with active syphilis can be "superinfected" with a heterologous strain of the same disease. Experiments have likewise shown that in spontaneous spirochetosis positive results may be obtained even with homologous strains.

Experiments with the infection of albino mice, rats, guinea-pigs, dogs, cats and monkeys invariably gave negative results. The experiments of Levaditi and Nicolau and of Danila and Stroe have shown that man likewise is not susceptible to spontaneous spirochetosis. On the contrary, syphilis of the rabbit can be transferred to the animals enumerated. Similarly, man (as shown by accidental laboratory infection reported by Buschel and others) is liable to contract the disease from the rabbit.

Study of the cerebrospinal fluid of rabbits with spontaneous spirochetosis as well as that of the serum has not contributed to the knowledge whether the disease represents a generalized infection or is merely

a local infection. The blood serum was investigated with the methods of Wassermann (as modified in the Institute) and Sachs-Georgi. Parallel studies were performed on rabbits free from any disease and also in those with syphilis.

Three hundred and ninety-three serums from animals with spontaneous spirochetosis showed a positive Wassermann reaction in 50 per cent, and a positive Sachs-Georgi reaction in only 34 per cent. The control syphilitic rabbits yielded positive reactions varying between 70 and 80 per cent, while the percentage of positive normal serums was negligible. It is also of importance that whereas in syphilis the strength of the reaction ran parallel with the clinical picture of the disease, in spontaneous spirochetosis we often obtained positive results with initial lesions and negative results with advanced lesions. This led us to the conclusion that the serodiagnosis in spontaneous spirochetosis most likely is not specific.

CHEMOTHERAPY

Neoarsphenamine, bismuth and mercury, used in the treatment for syphilis, are employed with equal success in spontaneous spirochetosis. However, the cure of the disease caused by Spirochaeta cuniculi requires much larger doses than that of experimental syphilis. Thus, in the latter 0.02 Gm. of neoarsphenamine, or 0.004 Gm. of the Russian silver arsphenamine, per kilogram of weight is required, whereas in spontaneous spirochetosis the dose is increased to from 0.06 to 0.08 Gm. of the first drug and to 0.01 Gm. of the second. Kolle, Ruppert and Möbius have utilized this property as a therapeutic test to distinguish between the two conditions. With the use of bismuth according to the method of Sazerac and Levaditi, the disappearance of the spirochete occurs much slower in spontaneous spirochetosis than in syphilis. On the other hand, Spirochaeta cuniculi is more susceptible to the action of acetarsone (stovarsol) than Spirochaeta pallida. From the literature it would appear that when the proper dose is used, one treatment will lead in most instances to a stable cure of the disease.

Our investigations can be summarized as follows:

1. In spontaneous spirochetosis the curative dose of neoarsphenamine and of the Russian neoarsphenamine varies from 0.060 to 0.080 mg. of the chemicals per kilogram of weight. When such a dose is used, the spirochete disappears from the lesion the following day, and the lesions disappear in periods varying from eight to fifteen or twenty-two days. In no instance did we observe recurrences of the disease. When smaller doses of these arsenic preparations are used, the therapeutic effect is either nil or only temporary.

2. The effect of preparations of bismuth on Spirochaeta cuniculi is much slower than that of neoarsphenamine, even in doses approaching the limits of tolerance. Thus, with the use of the highest possible doses of bismuth, the motility of Spirochaeta cuniculi ceased only on the third to the fifth day.

3. The Russian neoarsphenamine has a therapeutic effect on the Spirochaeta cuniculi equivalent to that of the German neoarsphenamine.

4. Spirochaeta cuniculi is much more resistant than Spirochaeta pallida to the preparations of arsphenamine and bismuth, which may be given to the same animal as a therapeutic test.

In general, our method of treatment for spontaneous spirochetosis consisted in a combination of arsphenamine and of bismuth. Arsphenamine was given intravenously in one dose varying from 0.080 to 0.100 mg. per kilogram of weight, this being followed about three weeks later by an intramuscular injection of from 0.7 to 0.9 mg. of bismuth (a 10 per cent emulsion of bismuth subsalicylate in olive oil) per kilogram of weight. A prophylactic treatment was also given to apparently healthy animals. As a result of this procedure the condition was not observed on our farm for a year and a half preceding this writing.

CONCLUSIONS

Spontaneous spirochetosis is an autonomous disease found in rabbits (and probably in the field hare).

The infection caused by the Spirochaeta cuniculi is transmitted from animal to animal by genital contact only, leading to a chronic disease of the skin in the anogenital region (and, in females, of the mucosa) and sometimes also of other parts of the body. The process is sometimes accompanied by a regional adenopathy.

The occasional presence of spirochetes in the tributary lymph nodes and also in the blood reported by some authors was not confirmed in these studies.

The Wassermann and the Sachs-Georgi reactions are, as a rule, negative in spontaneous spirochetosis.

Animals cured of spontaneous spirochetosis are susceptible to new infections.

Spirochaeta cuniculi causes no specific lesions in the viscera or in the central nervous system. Likewise the cerebrospinal fluid in this disease shows no cytologic or chemical changes.

Spontaneous spirochetosis is a local parasitic disease of the skin which may be generalized in rare instances.

It is believed that in spite of the morphologic identity of Spirochaeta cuniculi and Spirochaeta pallida, their biologic properties and the processes that they cause are entirely different. The two diseases can be differentiated by clinical and laboratory tests. In difficult cases the therapeutic test with bismuth or arsphenamine may be a reliable guide in the differential diagnosis.

This study has revealed (as others also have observed) that, not infrequently, apparently normal rabbits show changes of the viscera, central nervous system and cerebrospinal fluid which resemble those seen in advanced syphilis in man. The results obtained from the study of the syphilitic disease of these organs in the rabbit must, therefore, be accepted with reservations.

THE ANNULAR MACULAR SYPHILID (NEUROSYPHILID, UNNA)

FRANK C. COMBES, M.D.
NEW YORK

The annular macular syphilid, or the neurosyphilid of Unna, is one of the rarer manifestations of syphilis, and, oddly, one that is alluded to in only a few of the textbooks on dermatologic practice. The first case to be presented before a dermatologic society in this country was by Howard Fox [1] in 1917. The case herein presented agreed in its various manifestations with those previously described, but showed also some unusual lesions of the genitals.

Insufficient treatment for early syphilis is responsible for the reappearance of secondary cutaneous symptoms. These relapsing roseolas may recur several times during the first few years of the disease. Harttung [2] mentioned one patient, treated with mercury, in whom the syphilid recurred five times in three years, disappearing after each recurrence. Fournier [3] reported a case in which a relapse occurred eight times in four years.

The purpose of this communication is to describe annular macular lesions occurring in syphilis which, while clinically resembling those developing in early syphilis and in the relapsing roseola, are in reality not a cutaneous syphilid at all, in the histologic sense of the term, but rather a vascular manifestation of the disease. Their complete identity cannot be verified without a microscopic examination of the excised tissue, and then only when this is interpreted in correlation with the clinical features of the process.

There are about fifty cases in the literature of annular macular syphilid of this type, including those of Fournier,[3] Mauriac,[4] Jullien,[5]

Submitted for publication, May 27, 1931.

From the Department of Dermatology and Syphilology, University and Bellevue Medical College, service of Dr. Howard Fox.

1. Fox, Howard: The Annular Macular Syphilide, or So-Called Neurosyphilide, J. Cutan. Dis. **25**:215 (April) 1917.

2. Harttung: Beitrag zur Kenntnis der wiederkehrenden makulösen Syphilide, Arch. f. Dermat. u. Syph. **43**:307, 1898.

3. Fournier, A.: Roséoles syphilitiques à récidives multiples, Ann. de dermat. et syph. **7**:1141, 1896.

4. Mauriac, C.: Leçons sur les maladies vénériennes, Paris, J. B. Baillière et fils, 1883, p. 523.

5. Jullien, L.: Traité pratique des maladies vénériennes, Paris, J. B. Baillière et fils, 1899, p. 701.

Souplet,[6] Brauman,[7] Leistikow,[8] Neilsen[9] and von Zeissl.[10] Taylor,[11] Shillitoe,[12] Abraham and Davis[13] and Rothwell[14] have reported cases ostensibly of Unna's neurosyphilid, but the lesions were definitely not of this variety, but rather lesions of the early relapsing annular macular and annular papular types.

Stokes[15] reproduced in his text on syphilis an excellent illustration entitled "the so-called neurosyphilide of Unna, an annular papular type. Buschke,[16] in Riecke's textbook on skin diseases, inserted a very poor colored plate of an annular macular syphilid of the early relapsing type. The condition is extremely difficult to photograph, a fact that probably accounts for the dearth of illustrations in the literature. Two of the best reproductions are those of G. H. Fox[17] and Howard Fox.[1] A very excellent impression in wax may be seen at the Hôpital St. Louis, in Paris.

To Fournier belongs most of the credit for first describing this interesting process in detail, which he termed "érythème circiné tertiaire." This name was first suggested by Brauman in 1891. Fournier[18] gave due credit to Brauman for drawing attention to the condition in a brief comment on the occasion of the presentation of a case by Souplet. He admitted that he had seen this eruption from time to time for many years without recognizing it as syphilitic in origin. It was his firm opinion, after a review of the literature and his own observations,

---

6. Souplet, M.: Sur un cas d'érythème circiné tertiaire, Ann. de dermat. et syph. **3**:1151, 1892.

7. Brauman, J.: De l'érythème circiné tertiaire, Annales de la syphilis, Thèse de Paris, 1891.

8. Leistikow, L.: Zur Therapie der Neurosyphilid, Monatsh. f. prakt. Dermat. **18**:177, 1894.

9. Neilsen, L.: Circinäre syphilitische Erythema (Neurosyphilide-Unna), Monatsh. f. prakt. Dermat. **22**:500, 1896.

10. von Zeissl, M.: Roseolarecidiv 29 Jahre nach der Infection; 3 Fälle von Mastdarmsyphilis, Wien. med. Presse **34**:82, 1893.

11. Taylor, R. S.: A Practical Treatise on Genito-Urinary and Venereal Diseases, ed. 3, New York, Lea Bros. & Company, 1904, p. 542.

12. Shillitoe, A.: A Case of Circinate Erythematous Syphilide, Proc. Roy. Soc. Med. (Sect. Dermat.) **1**:21, 1907-1908.

13. Abraham, P. S., and Davis, H., in Power and Murphy: A System of Syphilis, New York, Oxford University Press, 1910, vol. 5, p. 38.

14. Rothwell, J. J.: Annular Macular Syphilis, J. Cutan. Dis. **36**:395 (July) 1918.

15. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, 1927, p. 472.

16. Buschke, A., in Riecke: Lehrbuch der Haut- und Geschlechtskrankheiten, Jena, Gustav Fischer, 1914, p. 658.

17. Fox, G. H.: J. Cutan. Dis. **21**:234 (April) 1913.

18. Fournier, A., in discussion of Souplet (footnote 6).

that the condition was separate and distinct from the relapsing early cutaneous efflorescences of the disease and should be classed as a late tertiary manifestation.

REPORT OF CASE

The woman (F. S.) on whom this report is based was 39 years of age and born in the United States. She gave the history of infection with syphilis through venereal contact fifteen years previously. She developed the usual early macular

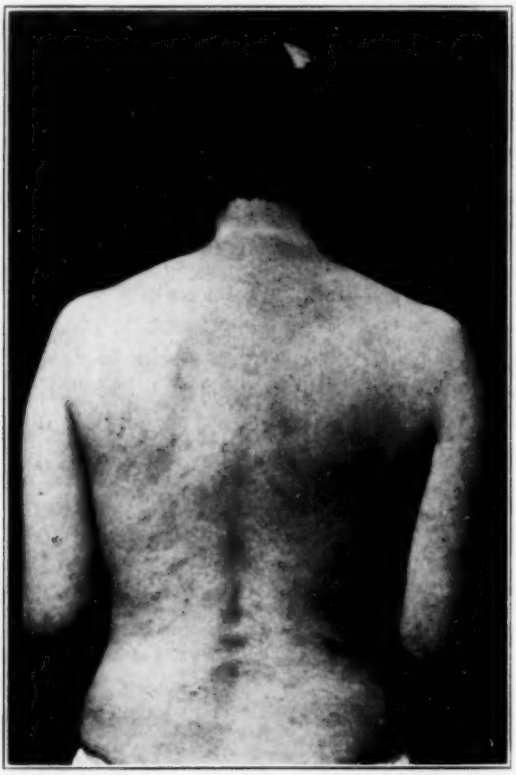

Fig. 1.—Annular macular syphilid (neurosyphilid of Unna).

roseola, at which time she received treatment for four months, consisting of six intravenous injections and approximately a dozen injections of what was probably a mercurial salt. A Wassermann test was not made at the completion of this short course of treatment, but the patient stated that she was greatly improved in health and that all evident manifestations of the disease had subsided. She had always partaken excessively of strong spiritous liquors.

In the fall of 1930 she visited the skin department of the University and Bellevue Medical College, when she first came under my observation. At that time she had a generalized erythematous eruption confined to the body and extremities, sparing the face. It was of six weeks' duration, during which time it had not changed

in appearance. The patient was positive that the individual lesions had not enlarged or regressed, and that no new lesions had appeared. On the body the eruption was more pronounced about the waist, particularly in the lumbar region; on the upper extremities it was evident only on the flexor surfaces of the forearms; on the legs there was very little to be seen except a few lesions on the buttocks. Over the chest the lesions were very distinct, but not quite as pronounced as on the abdomen.

The eruption consisted of irregularly oval, circular and gyrate rings of erythema surrounding centers of normal skin. They varied in size from 2 to 4

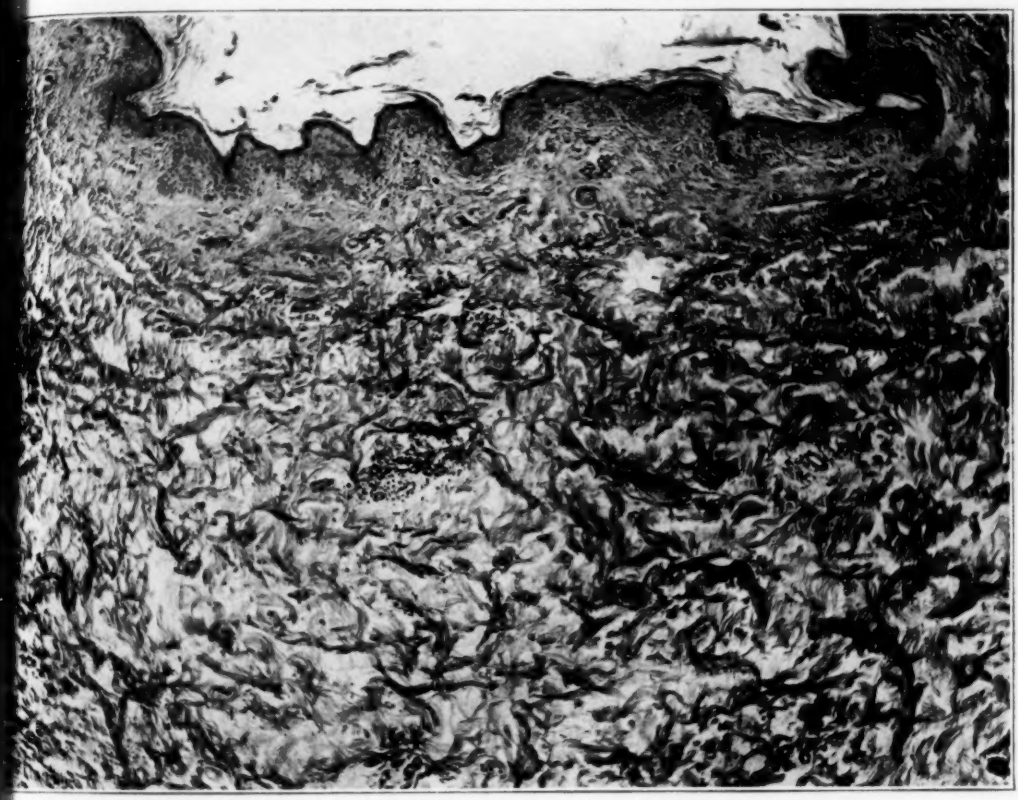

Fig. 2.—Low power photomicrograph showing the distribution of the infiltration.

cm., and in some instances the erythematous borders were in apposition, producing lesions from 6 to 8 cm. in diameter. The lesions were fewer in number and more irregularly disseminated than the early roseola of syphilis. They were not raised above the level of the skin, and there was no evidence of scaling or infiltration. They were a salmon pink. On pressure most of them disappeared completely, but in some a yellowish tinge remained.

In addition to the lesions described, the patient presented on either labium majus two superficial noninfiltrated soft lesions, each about 1.5 cm. in diameter. One of these formed a perfect ring of denudation with a normal center. One

formed a horseshoe-shaped lesion with a normal center. The other two were simply denuded areas. The bases of the lesions were clean and pink, exposing the corium to view and free from discharge and crusting. The labia minora were hypertrophied. There was no palpable glandular enlargement. All of the lesions appeared at the same time and did not enlarge or show a tendency to disappear while the patient was under observation without treatment for a period of two months. There was no evidence of cerebrospinal syphilis.

Fig. 3.—High power photomicrograph showing the type of infiltration.

Histologic Examination.—A section of the tissue was removed from one of the lesions and stained with hematoxylin and eosin.

Under low power magnification there was little deviation from normal except that the capillary network, particularly in the papillary layer, was surrounded by a very sparse infiltration.

Under high power magnification the epidermis was normal. There was a cellular hyperplasia of the vessel walls. This was particularly well developed in the superficial vessels. The lumina were narrowed. In some cases the vessel walls were twice the normal thickness due to the swelling of the endothelium.

Some looked almost like solid strands, the lumen being almost imperceptible. The perivascular infiltration was very sparse and well circumscribed and consisted of a few round cells and spindle cells. Many cells showed mitotic figures. There were no plasma cells present. The arterial capillaries seemed to be affected to a greater degree than the venous capillaries. There were no changes in the general appearance of the stroma.

The Wassermann reaction of the blood was positive. The spinal fluid was normal.

Fig. 4.—High power photomicrograph showing an arterial capillary with marked endothelial proliferation and partial occlusion of the lumen.

COMMENT

The neurosyphilid differs from the early syphilids in that it appears years after the infection. Neilsen mentioned cases in which the lesions appeared for the first time from fifteen to eighteen years after the initial lesion. One case was reported by von Zeissl twenty-nine years, and one by Brauman forty-six years, after infection.

There is evidently a decided tendency to relapse. Neilsen noted this occurring three or four times in some cases.

As regards sex, there seems to be an impression that the condition is more common in women. This, however, is only apparent, since Neilsen, who had seen probably more cases than other observers, made most of his studies at the Vestre Hospital for prostitutes. Unna [19] reported twenty-nine cases from the literature, nineteen occurring in men and ten in women.

The state of health of all the patients was apparently good, but most of them gave an alcoholic history and led a more or less irregular debilitated life.

The eruption has in many cases appeared concomitantly with gummas and tuberculosquamous syphilids. Wickham,[20] in a communication, noted an associated squamous syphilid of the hand in one case. Frequent reference is made to associated neurosyphilis although there is not sufficient evidence to say conclusively that a definite relationship exists between the two conditions. Nevertheless, it is the general opinion that such a relationship does exist.

The lesions make their appearance primarily as annular macules and do not change in size or configuration. In this respect they differ from the early annular macules which are rather evolutionary, the clear central areas resulting from peripheral extension of the erythematous border of the lesion resulting in a central paling. The lesions are always confined to the body and extremities. No cases are recorded in which they have been observed on the face, with the exception of one reported by Freund.[21] Those occurring on the trunk are usually more florid in appearance than those on the arms and legs.

The lesions are fewer than in the usual early roseola and are of greater diameter. Frequently the rings have measured several centimeters. Fournier saw rings as large as 8 cm., and Brauman reported a case in which the diameter of one lesion was 22 cm.

The color of the borders is usually pale pink. In some cases reported, this was frequently mixed with a yellow pigmentation which, according to Unna, sometimes remained as long as a year after the erythema had receded. The color is less pronounced than in the common macular roseola. The central area is usually normal in appearance, but some cases have occurred in which there were dyschromic changes that resulted in hyperpigmentation or vitiliginous areas which

19. Unna, P.: Neurosyphilides et neuroléprides, J. d. mal. cutan. et syph., August-September, 1889, vol. 1.

20. Wickham: Correspondence, Monatsh. f. prakt. Dermat. **5**:464, 1891.

21. Freund, E.: Gior. ital. di dermat. e sif. **66**:1248 (Aug.) 1925.

remained for several years. Unna [22] attempted to establish a relationship between the genesis of the neurosyphilid and that of the so-called pigmentary syphilid of the neck first described by Hardy [23] in 1853.

He considered the neurosyphilids as analogous to the neuroleprid, and separated them on a clinical and histologic basis from the other syphilids which correspond to the cutaneous lepromas. His classification included: (1) erythematous neurosyphilid (érythème circiné tertiaire, Brauman), (2) erythematopapular neurosyphilid (Unna), (3) erythematopigmented neurosyphilid (Unna) and (4) primary pigmented neurosyphilid (Hardy).

As a rule, the lesions are entirely erythematous and devoid of any scaling or infiltration, although Wickham, Brauman, Unna and others have described sporadic cases with slight scaling and some papular elements. Unna considered the latter variety a distinct type and designated it as the annular papular type of neurosyphilid. Neilsen also observed that some of the lesions appeared to be slightly raised. The erythema varies in intensity with the temperature of the skin. Friction makes it more prominent. Unna placed great emphasis on this characteristic in his differentiation of the condition from the ordinary cutaneous syphilids.

There are usually no subjective symptoms accompanying it. The unobservant patient is unaware of its presence. Some of the patients have complained of headache of associated cerebrospinal syphilis. As a rule, there is no generalized adenopathy.

One of the essential characteristics is the tendency of the lesions to persist, unchanged, whether or not the patient is treated. In the majority of the cases reported, the ordinary anti-syphilitic remedies had little effect on the eruption. It was not unusual for it to remain in spite of treatment for over a year. Brauman reported one case in which it persisted unchanged for over five years. Considerable emphasis has been placed on local applications, such as inunctions and mercurial plasters. Quinquard [24] had good results with mild mercurous chloride plasters. Leistikow found that the eruption responded better to reducing agents, such as chrysarobin and pyrogallic acid. He used a 5 per cent chrysarobin plaster or an ointment containing 10 per cent pyrogallol. He also obtained results in some cases using a 20 per cent alcoholic solution of pyrogallol. Vidal [25] advocated an ointment of yellow mercuric oxide in addition to general treatment with mercury.

22. Unna, P.: Histopathology of the Diseases of the Skin, translated by Norman Walker, Edinburgh, W. F. Clay, 1896, p. 124.

23. Hardy, A.: Maladies de la peau, Paris, A. Delahaye, 1858, p. 154.

24. Quinquard, in discussion of Souplet (footnote 6).

25. Vidal, in discussion of Souplet (footnote 6).

Buschke is of the opinion that the condition responds better to mercury than to arsphenamine. In the case herein reported there was a prompt response to neoarsphenamine.

There seems to be considerable difference of opinion as to the relationship between previous treatment and the incidence of the neurosyphilid. According to Bazin [26] and Bassereau,[27] it did not occur in those patients who had taken mercury. Neilsen subsequently disproved this, as many of his patients developed lesions while under mercurial treatment.

In reference to the genital lesions, I have found no mention of them in the literature. Wickham referred to a patch on the tongue, devoid of papillae, in one case of Fournier's, but with this exception no lesions of the mucous membranes have been reported.

The apparent rarity of the condition may be readily explained. In the first place the eruption may be so faint as to escape notice, particularly in the absence of any subjective symptoms. Secondly, as it comes so long after the initial infection and because of its unusual and picturesque appearance, syphilis may not be suspected. It is most likely to be confused with erythema multiforme, pityriasis rosea, pityriasis versicolor, trichophytosis, seborrhea corporis and leprosy. From the cutaneous syphilids it may be differentiated by the fact that it is purely a circulatory disturbance and the clinical appearance is due solely to changes in the vascular network of the skin. Other classic characteristics are the complete absence of infiltration, the stability, chronicity and slow response to therapy.

---

26. Bazin, A. P. E.: Leçons théoriques et cliniques sur la syphilis et les syphilides, Paris, A. Delahaye, 1866, p. 282.

27. Bassereau: Traité des affections de la peau symptomatiques de la syphilis, Paris, J. B. Baillière et fils, 1852.

A CASE OF XERODERMA PIGMENTOSUM

WITH SPECIAL PIGMENT STUDY

S. WILLIAM BECKER, M.D.
CHICAGO
AND
L. M. PAUTRIER, M.D.
AND
F. WORINGER, M.D.
STRASBOURG

Xeroderma pigmentosum is a well known condition, concerning which an extensive literature has accumulated. In recent years, the cases have been studied from the functional standpoint, as regards both cutaneous hypersensitiveness and pigmentary disturbance.

Martenstein [1] studied a patient, and found hypersensitiveness to ultraviolet, alpha and roentgen rays. No sensitivity was elicited to infrared and visible rays or to chemical irritants. In a second patient, Martenstein and Bobowitsch [2] found hypersensitiveness to all types of rays. Juon [3] found hypersensitiveness to ultraviolet and roentgen rays. That the pigmentation is merely a secondary phenomenon is suggested by the case reported by Audry.[4] A man, aged 24, with an inoperable carcinoma of the lower lip, was seen. The skin presented the marked changes found in xeroderma pigmentosum, namely, atrophy and telangiectasia. The condition had been present since infancy. The hair was brown. No pigment, crust or verrucae were seen. After a few days of treatment, a few pale ephelides could be seen on his hands.

Submitted for publication, June 22, 1931.

From the Division of Dermatology of the Department of Medicine of the University of Chicago and the Dermatological Clinic of the University of Strasbourg.

1. Martenstein, H.: Experimentelle Untersuchungen über Strahlungempfindlichkeit bei Xeroderma pigmentosum, Arch. f. Dermat. u. Syph. **147**:499, 1924.

2. Martenstein, H., and Bobowitsch: Ueber Strahlenempfindlichkeit bei Xeroderma pigmentosum (Untersuchungen an einem weiteren Fall), Arch. f. Dermat. u. Syph. **150**:165, 1926.

3. Juon, M.: Beitrag zu den experimentellen Untersuchungen über Strahlenempfindlichkeit bei Xeroderma pigmentosum, Arch. f. Dermat. u. Syph. **156**:367, 1928.

4. Audry, C.: Sur un cas de xeroderma pigmentosum sans pigmentation, Ann. de dermat. et syph. **8**:199, 1907.

The most complete pigment studies reported are those of Bertaccini.[5] He studied sections by the dopa reaction, and studied the cutaneous reactivity to various rays. The illustrations accompanying the report illustrate normal and pathologic skin. The normal skin showed many dopa-positive cells in the basal portion of the epidermis, but little visible pigment. The pathologic section showed considerable pigment, with a slightly positive dopa reaction; the cells showed no branching. This apparent inactivity may be due to the particular stage of the process.

The following case was studied by modern pigment methods.

REPORT OF A CASE

History.—A boy, aged 6, was observed at the dermatologic clinic of the University of Strasbourg, on July 2, 1930. His mother had died, probably of pulmonary tuberculosis. His parents were first cousins. Four sisters were well, and one sister had died at the age of 8 months, probably of pulmonary tuberculosis. One brother had died suddenly at the age of 5 months, of an unknown cause. No trouble similar to that of the patient was found in the sisters. The patient had been treated at the age of 6 weeks in the Pediatric Clinic, for digestive disturbance. No dermatosis had been noted at that time.

At the age of 6 months, freckle-like lesions had appeared, first, on the face, then on the hands. The pigmentation was limited to the parts exposed to light. Some time later, photophobia was noticed; it became more and more marked. Lesions appeared on the legs when sox were worn, and disappeared when long stockings were worn.

Physical Examination.—The child presented a pitiful appearance, and was somewhat thin. General examination showed nothing abnormal, and a test for porphyrin in the urine was negative. The lesions occupied the face, neck, ears, a little of the scalp, especially the temporal region, the backs of the hands and the wrists. Photophobia was intense, necessitating dark glasses, which afforded only partial relief.

The lesions occupied the entire face from the hairline to the inferior portion of the neck (fig. 1), where the lesions were sharply limited at the level of the shoulders. The ears and nape of the neck were also involved. In this region the skin presented a medley of tints, rose, red and brown. An erythematous base could be distinguished, less marked at the forehead and accentuated in the region of the nose and cheeks, varying from pale rose to deep red. On this background was seen a peppering of pigmentary spots, almost confluent in places, ranging from 1 to 3 mm. in diameter, varying from *café au lait*, through grayish to blackish brown, the predominating color being brown. The lesions were for the most part circinate, but some of them were irregular and confluent, producing figures of varying form.

In certain regions, the skin had a slightly atrophic aspect, and in places was definitely cicatricial; the cicatricial portions varied from 1 to 3 mm. in diameter. In some regions, especially on the nose, the skin was slightly verrucous and crusted, and small cornified excrescences could be seen from 2 to 3 mm. in size.

---

5. Bertaccini, G.: Xeroderma pigmentoso, richerche, cliniche esperimentali, Gior. ital. di dermat. e sif. **68**:1152, 1927; Nuovo osservazioni sopra un caso di xeroderma pigmentoso, ibid. **70**:3, 1929.

On the right lower eyelid was a small, elevated tumor 3 by 4 mm. in size, slightly ulcerated, bleeding easily, and having all the characteristics of a small vegetating carcinoma.

The vermilion borders of the lips were mottled with brown-black pigmented plaques on a membrane a little pale in places, as if cicatricial, with small, slightly ulcerated, and small purpuric, points. The submaxillary and cervical glands were enlarged.

On the scalp were small pigmented lesions, more discrete and less important than those on the face, possibly owing to the fact that the scalp was partially protected by the hair.

Fig. 1.—Lesions on the face and neck.

Lesions were marked on the dorsal surface of the hand (fig. 2), becoming less marked on the dorsa of the fingers, where they disappeared toward the terminal phalanges. From the back of the hand, the lesions extended to the dorsum of the wrist, where they were marked, fading out toward the center of the forearm; they extended to the external and internal surfaces, and a very little on the extensor surface. The palms were normal. On the back of the hand the lesions were confluent, and appeared much as on the face. On palpation, the skin was rugous and presented small papillary verrucosities, 2 mm. in diameter. As the lesions faded out above and below, only pigmentary macules were present, without erythema.

To sum up, the eruption consisted of a mixture of erythema, confluent pigmentary spots, telangiectases and atrophic macules; it was suggestive of radiodermatitis, but differed in the intensity of the lesions and in the distribution of the macules.

Microscopic Examination.—Two sections were removed for biopsy, one from the back of the hand and one from the nape of the neck. The sections from the hand were stained, and those from the nape of the neck were used for the dopa reaction.

Ordinary staining revealed a thickened epidermis, especially in regions with marked dermal inflammation. The thickening involved almost exclusively the stratum corneum, which was about as thick as the rest of the epidermis. This thickened stratum corneum was dense and adherent. In the more inflamed regions, it was still thicker and parakeratotic. In these places, the stratum granulosum became thin and finally disappeared, while in regions showing simple hyperkeratosis it was thickened and comprised about five layers of cells. The stratum mucosum showed only slight intercellular edema, with immigration of some lymphocytes where the inflammation was most marked. In places in the stratum mucosum, the cells appeared compressed and presented rare monstrosities, such as binucleated or trinucleated cells, prominent by their large size. The basal layer presented differences, depending on the regions examined. In the less inflammatory regions, the epidermodermal junction was regular and normal,

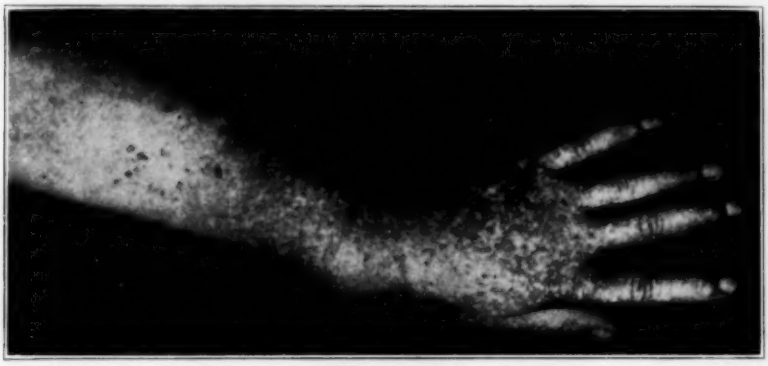

Fig. 2.—Lesions on dorsum of left hand.

but where the dermis was considerably infiltrated the basal cells showed more marked and edematous intercellular spaces, and the epidermodermal boundary was distorted by the infiltration. The interpapillary prolongations appeared smaller throughout, except in the regions showing dermal infiltration, where they were elongated, edematous and irregular.

The papillae and superficial dermis showed inflammatory changes throughout in varying degree. Marked in certain regions, the inflammation involved the epidermal modifications already described; elsewhere it was moderate, becoming slight in places. It consisted of cellular infiltration, histiocytes and fibroblasts largely predominating, with some lymphocytes and rarely mast cells. This infiltration was accompanied by vasodilatation and by new formation of capillaries in the papillary and subpapillary network. Certain of these capillaries were ectatic, forming true cisterns, which explains the telangiectasis in the clinical picture. In the inflammatory regions, the elastic tissue was lacking, although it appeared normal elsewhere. The deeper dermis was normal, except for some vasodilatation, as well as the sweat glands and pilosebaceous structures.

The silver nitrate reaction showed the presence of pigment in large quantity, but intermittently. The most inflamed regions generally contained less, but other

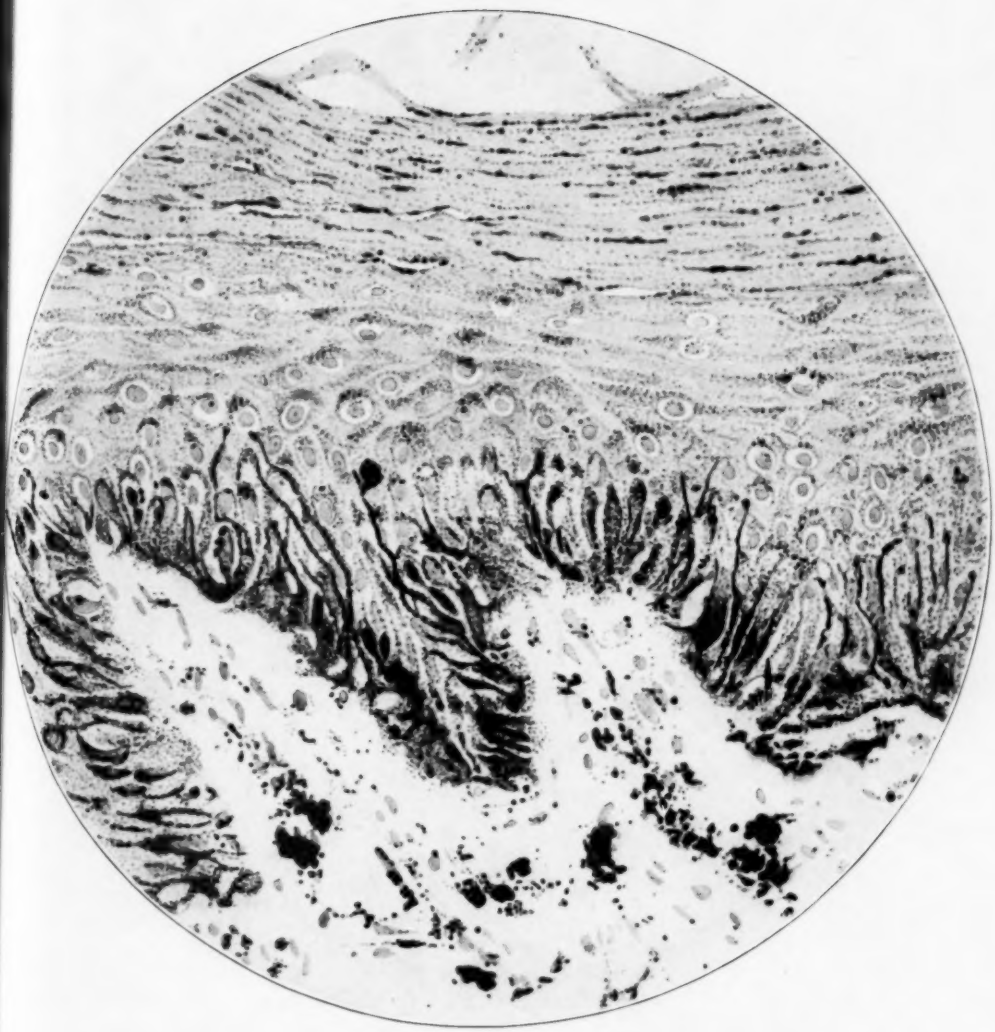

Fig. 3.—Marked pigmentation, both in epidermis and dermis. Numerous melanoblasts with branches are seen. Oil-immersion lens; silver nitrate reaction, pyronin methyl-green stain.

UNIV. OF MICH.

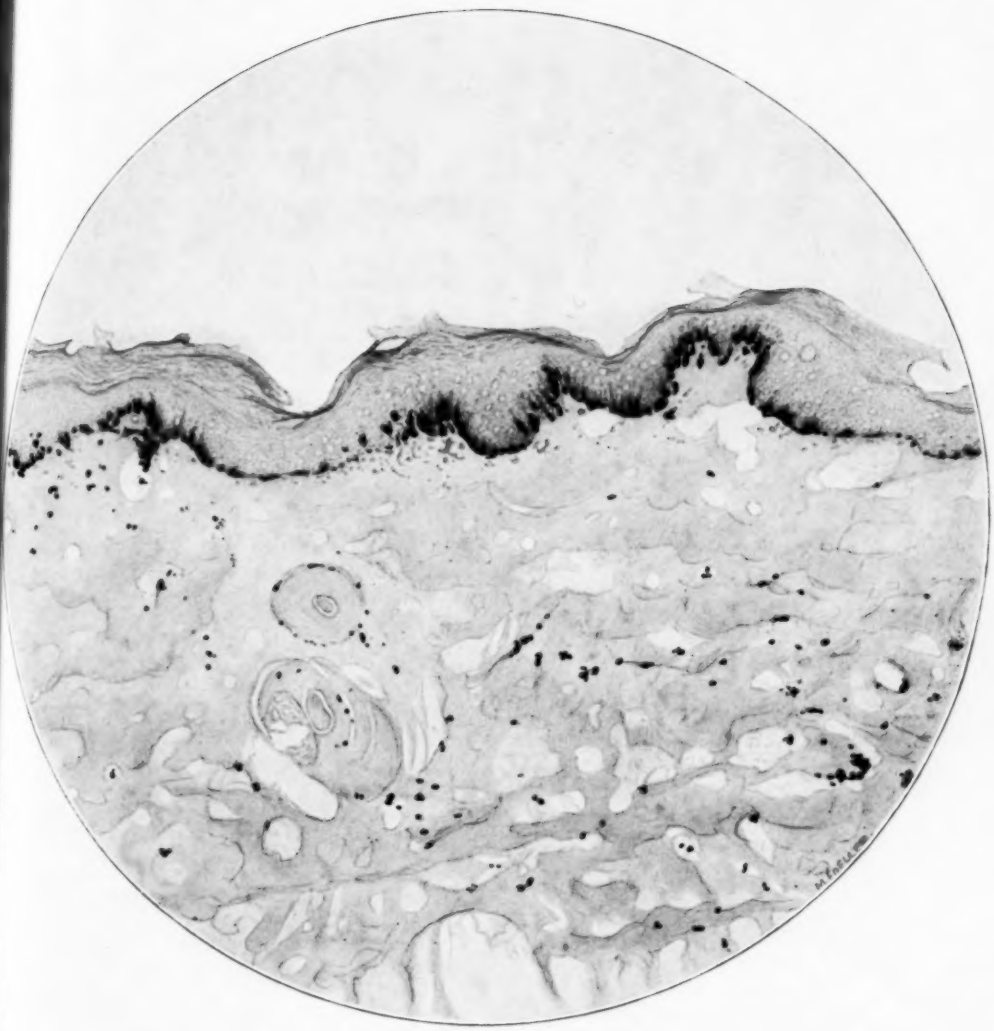

Fig. 4.—The dopa reaction is intermittent, being most marked in regions with the greatest amount of dermal pigment. Note that the phagocytic melanoblasts of the dermis do not show a positive reaction; low power magnification, dopa reaction; no counterstain.

UNIV. OF MICH.

regions also were absolutely deprived of pigment. This lack of pigment was variable in extent up to a few millimeters, ceasing abruptly or gradually, as shown in the clinical picture. In the pigmented area, most of the pigment was in the basal layer of the epidermis and in the adjacent layers. In the markedly pigmented regions numerous dendritic melanoblasts were seen (fig. 3). They were located in the basal layer of the epidermis, and their cell bodies often projected into the dermis. In contrast to the basal malpighian cells, which were seen particularly well in Masson's trichrome stain, the melanoblasts were distinctly separated by a clear space, probably due to an artefact, such as retraction of the protoplasm by the fixing fluid. The pigment granules permitted one to follow their protoplasmic prolongations, which extended along the basal layer and sent branches into the epidermis. In the Masson trichrome stains the melanoblasts could be readily recognized, even when they contained very little pigment. With this stain, their cellular structure appeared more distinct, their nuclei in general opaque, with one or two large nucleoli of an irregular form, perhaps due to retraction. The protoplasm was definitely different from that of the basal cells. It was a little basophilic, presented a finely alveolar structure and lacked protoplasmic filaments. The clear space surrounding it showed no intercellular bridges. The basal cells were not excessively pigmented, but the more superficial cells presented unusual quantities of pigment, which was present even to the surface. It was present in the form of the usual round or oval granules. Much pigment was found in the chromatophores of the papillae and superficial dermis, in the form of irregular lumps and clods. In the slightly pigmented plaques, that is, principally the very inflammatory regions, pigment was present in a few dendritic melanoblasts and in the adjacent cells.

The dopa reaction was marked but intermittent (fig. 4). It was more strongly positive in the more markedly pigmented regions, where the positive cells were close together. Short branches could be seen. In the less pigmented regions, the dopa-positive cells were separated, and in places they were absent for a considerable space. It is necessary to remember that this intermittent and marked pigmentation does not actually represent the maximum activity. The branches of the melanoblasts were short. The patient had been protected from the sun's rays for some time, which could explain the slightly decreased activity from the maximum.

The tumor of the eyelid was not of particular interest. It consisted histologically of a chronic telangiectatic granuloma with numerous lymphocytes and some polymorphonuclear cells in diapedesis and in the perivascular tissue. The tumor was for the most part ulcerated and covered by a crust. The epidermis, where present, was budding and hyperplastic, with some atypical cells and without definite carcinoma formation.

The intricacy of the lesions of pigmented, erythematous and pale lesions made it impossible to study each type histologically. It is certain, however, that pigmentation was intermittent. The marked epidermal pigmentation produced the brown color and masked the dermal pigment, which would otherwise produce a slate gray hue. The inflammatory lesions produced the erythematous and telangiectatic lesions. The white lesions followed the inflammatory changes. We could not find atrophic lesions microscopically.

COMMENT

We know nothing concerning the essence of xeroderma pigmentosum, and our complete microscopic study does not advance our

knowledge a great deal. We do not know to what is due this congenital hypersensitiveness to solar rays, in particular to ultraviolet rays, as many authors have shown. The patient with xeroderma pigmentosum responds by an exaggerated inflammatory reaction to the radiations and secondarily by pigmentation in most cases.

SUMMARY

A case of xeroderma pigmentosum was studied by modern methods of pigment study. The brown color of the lesions is due to a large amount of epidermal pigment. The dopa reaction is intermittent, as is the degree of pigmentation. The pigmentary process seems to be secondary to an inflammatory change.

DERMATITIS FROM CINNAMON

LOUIS TULIPAN, M.D.
Assistant Clinical Professor of Dermatology and Syphilology, New York University Medical School
NEW YORK

Since the advent of the patch test in determining cutaneous susceptibility to external irritants, many substances have been added to the list of proved causes of dermatitis. An examination of the literature [1] concerning dermatoses from external irritants revealed no mention of cinnamon as a possible cause.

The following case is presented as a dermatitis due to cinnamon.

REPORT OF A CASE

E. G., a white man, aged 33, was seen with an eruption on the hands. He had been a baker for nineteen years and had had an eruption on his hands only once before, seven years prior to examination, which had healed spontaneously after three weeks. His duties consisted in preparing the dough and icing for pies and cakes, as well as their final baking. Four days before the onset of the eruption, he had changed his position, although his duties were the same.

On examination, about eight weeks after the onset of his illness, he presented a pinhead-sized vesicular eruption on erythematous bases with fissuring and crusting. Both palms from the finger tips to the wrists were involved.

In the preparation of the dough and icing, the following ingredients were used: flour, baking powder, cream of tartar and cinnamon sugar. Patch tests performed with these four substances showed a positive reaction only to cinnamon sugar. A patch test with dough also gave negative results. Further tests with cinnamon and cane sugar separately proved cinnamon to be the sole offender. A very marked vesicular eruption was produced. Scales from the lesions on the palms were examined microscopically and culturally. Neither method showed fungi. Trichophytin tests performed intracutaneously and percutaneously gave negative results.

COMMENT

Although no instance could be found in the literature of a dermatitis due to cinnamon, White [2] reported the case of a girl who developed erythema and vesiculation on the hands, abdomen and face from the

Submitted for publication, June 5, 1931.

1. White, R. Prosser: The Dermatergoses or Occupational Affections of the Skin, New York, Paul B. Hoeber, Inc., 1929. Weber, L.: A List of Cutaneous Irritants, Arch. Dermat. & Syph. **21**:757 (May) 1930. List of Irritating Plants in the United States, Compiled by Bureau of Plant Industry, Department of Agriculture, March, 1923.

2. White, C. J.: Boston M. J., 1897, p. 78; quoted by White, R. P. (footnote 1).

Fig. 1.—Dermatitis of the hands, caused by cinnamon.

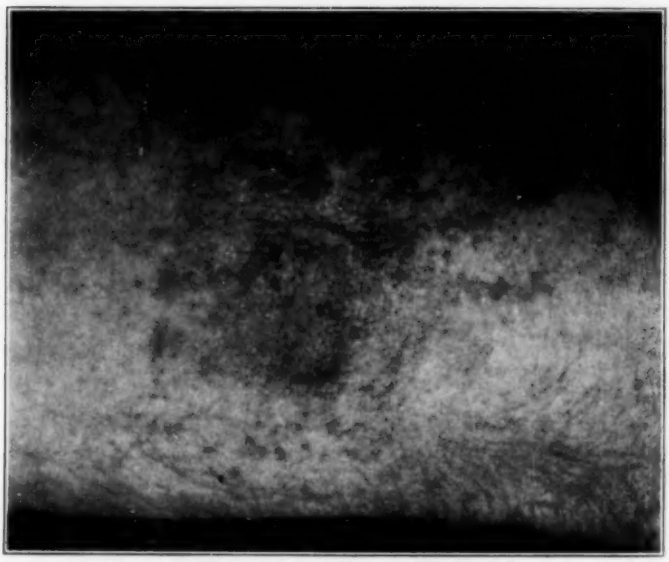

Fig. 2.—Reaction from a patch test on the flexor surface of the forearm.

use of oil of cassia as a substitute for oil of cinnamon. She had dipped tooth picks into the oil to produce a pleasant flavor.

Cassia and cinnamon are quite similar. True cinnamon [3] is produced from the dried bark of Cinnamomum zeylanicum, while cassia comes from Cinnamomum other than zeylanicum. Cinnamon powder contains from 1 to 1.5 per cent of the essential oil, which when fresh is a golden oil of aromatic odor and pungent taste. It is powerful enough to blister the tongue. Its chief constituent is cinnamic aldehyde (C_6H_5-CH:CH-CHO). The powder also contains starch, resins, pigments, tannin and some salts. Oil of cassia also contains cinnamic aldehyde as its chief constituent.

While cinnamon oil is irritating enough to blister the mucous membrane in normal persons, cinnamon powder is not a skin irritant ordinarily. The oil is a 60 to 70 per cent solution of cinnamic aldehyde, whereas the powder contains only from 0.9 to 1 per cent aldehyde. Although this concentration is bland to some skins, in the case of the baker it was sufficient to cause a marked dermatitis. The fact that the patient manifested his sensitivity after about nineteen years of contact is at present inexplicable.

I feel justified in calling this case a dermatitis due to cinnamon for the following reasons: Microscopically and culturally, and also by a trichophytin test, fungus was proved to be absent; patch tests with all ingredients used in baking gave negative results except with cinnamon; repeated tests with cinnamon gave positive results. The reason that lesions were present only on the palms and not on the dorsa is that the patient in spreading the cinnamon over the pie crusts scooped up the powder and sprinkled it from the palmar surface of his hands.

3. Wood, A. G.: Food Analysis, New York, McGraw-Hill Book Company, Inc., 1915, p. 34.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

THE DIAGNOSIS OF CONGENITAL SYPHILIS IN THE NEW-BORN. E. C. DUNHAM, Am. J. Dis. Child. **43**:317 (Feb.) 1932.

Dunham points out that a positive Wassermann reaction in an infant born of a mother with a positive Wassermann reaction does not necessarily mean congenital syphilis. It is entirely possible that a passive transference of complement-fixing substances may occur from mother to infant in utero. She points out that Cooke has observed a similar transference of antibodies in tuberculosis.

Hence in a series of fourteen cases, in which the first reaction of the infant's blood was positive either by the Wassermann reaction (alcoholic or cholesterolized antigen) or by the Kahn reaction, treatment for syphilis was withheld if the mother had had antisyphilitic treatment, even though the treatment was inadequate or given in the latter part of pregnancy. Treatment was also withheld in cases in which the mother, though known to have been infected during or before a previous pregnancy, had already given birth to a nonsyphilitic infant since the date of her infection.

Under such conditions, treatment of the infant who is free from symptoms or signs of syphilis has been withheld, regardless of the first Wassermann reaction, until the test could be repeated one or more times and evidence obtained with regard to the change in the strength of the reaction.

In the fourteen cases studied, the second or third blood test was usually weaker, and finally the blood gave a negative reaction. This negative reaction was usually obtained before the infant left the hospital in from ten to fourteen days.

These patients have been kept under careful observation for from two months to four years, during which time they have remained clinically and serologically normal.

AN IMPROVED PROTECTIVE DEVICE IN THE TREATMENT OF INFANTILE ECZEMA. J. V. GREENEBAUM and G. M. KEITH, Am. J. Dis. Child. **43**:387 (Feb.) 1932.

This device consists of two pieces of cellophane, one of which, measuring 16 by 20 inches (40.6 by 55.5 cm.), is fastened to the bed by strips of adhesive tape. This forms the piece on which the head rests. The other piece, measuring 14 (35.5 cm.) by 16 inches, has a hole 3¼ inches (9 cm.) in diameter cut in its center, with an opening extending from the circle to the edge of the cellophane. All the edges are bound with adhesive plaster. This piece is placed on the child, his neck fitting into the central opening, and the edges are brought together in the back and fastened with adhesive type. With the arms and legs restrained, the face is protected from rubbing because of lack of resistance of the cellophane.

ANDERSON, Los Angeles.

THE NATURE OF ALLERGY IN TUBERCULOSIS AS REVEALED BY TISSUE CULTURE STUDIES. A. R. RICH and M. R. LEWIS, Bull. Johns Hopkins Hosp. **50**:115 (Feb.) 1932.

The washed cells of the allergic, tuberculosis body have been shown to retain their hypersensitivity to tuberculin when isolated from the body in tissue cultures. It is therefore clear that neither circulatory, nervous nor other mechanisms dependent on the intact body are necessary for the production of allergic damage.

Cellular injury and necrosis associated with allergy in tuberculosis result from a change in the individual fixed tissue and blood cells, which renders them hypersensitive to the protein of the tubercle bacillus. This change, in all probability, consists in the intimate attachment of the antibody to the cells. Free, circulating antibody is not necessary for the production of the immediate, local injurious effects of allergy in tuberculosis.

AUTHORS' SUMMARY.

STUDIES IN URTICARIA: THE INFLUENCE OF METABOLIC FACTORS. LEO H. CRIEP and L. WECHSLER, J. Allergy **2**:479 (Sept.) 1931.

The authors report their findings in a study of the functional state of the gastro-intestinal tract and of the basal metabolism in forty cases of urticaria, and also review the literature on the subject. Only eight of their patients were free from gastro-intestinal disturbance, the remainder showing some involvement, such as constipation, gastric hypo-acidity or gallbladder disease. The authors feel that functional disturbances of the gastro-intestinal tract in an allergic patient cause an increased permeability, whereas in a normal person they may produce no disturbance.

Deviations from normal in the basal metabolism occurred in 35 per cent of the patients, but most of these had borderline cases of urticaria, and the condition is probably not important as an etiologic factor.

GLUE SENSITIVITY. GEORGE C. ANDREWS and C. W. MCNITT, J. Allergy **3**:30 (Nov.) 1931.

This is a report of a case of sensitivity to glue manifested by asthmatic attacks and by swelling of the tongue and lips. These attacks occurred after contact with fish glue and after eating fish. A severe reaction was obtained by performing a scratch test with a fish glue. The authors believe that most allergic reactions to glue depend on fish protein alone.

The most satisfactory treatment is complete removal of the offending source. Treatment by injections of glue allergen may also be instituted, but the dilution of the allergen must be very great to avoid systemic reaction.

CARO, Chicago.

EXPERIMENTAL LESIONS IN MONKEYS AND CULTIVATION OF BACILLUS LEPRAE. EARL B. MCKINLEY and MALCOLM H. SOULE, J. A. M. A. **98**:361 (Jan. 30) 1932.

In this article the authors report results of experiments that apparently are a step forward in the fulfilment of the postulates of Koch as regards Bacillus leprae. 1. They were able to produce granulomatous lesions suggestive of early lesions of leprosy in two species of monkeys, which was done by means of intradermal inoculation with human leprosy material. 2. They cultivated acid-fast bacilli (Hansens' bacilli) from human leprosy nodules on artificial mediums. 3. They produced granulomatous lesions in monkeys by intradermal inoculation with organisms from this culture material. The experiments are described in detail, and the literature on the subject is reviewed.

LABORATORY INFECTION IN MAN BY THE SPIROCHAETA PALLIDA OF EXPERIMENTAL RABBIT SYPHILIS. G. E. WAKERLIN, J. A. M. A. **98**:479 (Feb. 6) 1932.

A laboratory assistant accidentally brushed his hand against a needle attached to a syringe that contained a suspension of organisms prepared from syphilitic rabbit testicular tissue. The suspension contained approximately three organisms to a dark field. Four weeks later a mild arthritis of the wrist developed, and five weeks after that a generalized eruption typical of syphilis and a 4 plus Wasser-

mann reaction of the blood occurred. No chancre was visible. Six months previously the patient had been thoroughly examined, and there had been no evidence of syphilis. He was a man of 65, with a family, and other sources of infection could be definitely eliminated. The strain of spirochete with which he was infected had been carried in rabbits for thirteen years.

SENSITIZATION DERMATOSES OF NONFUNGOUS NATURE FOLLOWING SUPERFICIAL FUNGOUS INFECTIONS OF THE EXTREMITIES. CLEVELAND WHITE and SAMUEL J. TAUB, J. A. M. A. **98**:524 (Feb. 13) 1932.

This is a report of four cases that illustrate a type of sensitization dermatoses that has not been sufficiently emphasized. The patients presented themselves with sensitization dermatoses due to chemical or nonvital substances, the nature of which was determined by cutaneous tests, etc. The onset in each case followed attacks of superficial ringworm of the extremities. The cases illustrate the principle that one type of dermatitis may predispose the patient to another type, that the skin is made allergic by the one irritant, and that other allergens are then able to set up a dermatitis.

IODOBISMITOL. P. J. HANZLIK, H. G. MEHRTENS, CHARLES GURCHOT, C. C. JOHNSON, JEAN SPAULDING and D. C. MARSHALL, J. A. M. A. **98**:537 (Feb. 13) 1932.

Iodobismitol is a soluble bismuth product for use in the treatment of syphilis. It contains the bismuth as anion (most bismuth preparations contain the metal as cation), and it is therefore able to penetrate brain tissue. In this preliminary report, iodobismitol is said to be well tolerated locally and systemically, to be fairly rapidly absorbed and excreted, to possess antisyphilitic action, to penetrate the brain of animals and to appear in the cerebrospinal fluid of human beings. It is injected intramuscularly in doses of 2 cc. (equal to 0.023 Gm. of bismuth), and it is suggested that a course of treatment consists of ten injections over a period of three weeks. The authors think it is worthy of further clinical trial, for it offers the possibility of early treatment of syphilis and of prevention of neurosyphilis. The work is described in detail.

SERUM TREATMENT OF TULAREMIA. LEE FOSHAY, J. A. M. A. **98**:552 (Feb. 13) 1932.

In a very short preliminary report, results are given in ten cases of acute tularemia in which antiserum prepared from a goat inoculated with formaldehyde-killed suspensions of Pasteurella tularensis had been given. Ten cubic centimeters of the serum was given intravenously on the first and second days. No reactions occurred, and in every case but one, in which the patient was moribund when treated, there was prompt cessation of symptoms.

RATTNER, Chicago.

OBSERVATIONS ON THE ETIOLOGY OF ERYTHEMA EXUDATIVUM MULTIFORME. G. H. PERCIVAL and H. J. GIBSON, Brit. J. Dermat. **43**:329 (July) 1931.

The authors state that there are two views regarding the etiology of erythema exudativum multiforme. The first recognizes a true disease entity, the cause of which, as yet undiscovered, is provisionally held to be the same in all cases; the second regards erythema multiforme as a cutaneous manifestation of a large variety, as yet unexhausted, of intoxications and infections. The views are briefly discussed, and reference is made to the communication by Ramel in which the view is expressed that true erythema multiforme is a cutaneous tuberculous manifestation due to a scanty tuberculous bacillemia in an otherwise healthy subject.

A detailed review of Ramel's experimental work is given, together with a critical discussion. Then follows the detailed report of a similar investigation,

by the authors, in a series of ten cases of erythema multiforme and of six cases of other types of cutaneous disease as controls. Palmar and plantar hyperkeratosis, dermatitis, chronic ulcers of the leg, psoriasis, acne vulgaris and impetigo contagiosa were included in the six cutaneous diseases.

In ten cases of erythema exudativum multiforme cultures of the blood carried out during the period of active spread of the disease were entirely negative. Inoculation of guinea-pigs having negative reactions to tuberculin with blood from these cases, followed by successive inoculation with extracts of the viscera of these animals into other animals with negative reactions to tuberculin, according to the method of Ramel, did not give rise to tuberculous lesions in the latter animals. The early nonspecific lesions described by Ramel were not observed. No positive tuberculin reactions were found to develop. The animals that survived thrived normally, and maintained or increased their weight during the course of the experiment.

The investigations carried out by the authors failed to confirm the results obtained by Ramel, on which is based his theory of the tuberculous nature of all cases of true or idiopathic erythema exudativum multiforme. The cases investigated in the present research corresponded exactly in all clinical details to those of Ramel's series, and the technic he employed was not varied.

Percival and Gibson feel that the experimental results obtained by Ramel can be correlated with those of the present investigation only by discarding the hypothesis that erythema exudativum multiforme is a true morbid entity with but one cause and reverting to the conception that the entity is a cutaneous reaction capable of being produced by a variety of agents. It was also noted that in their experiments no organisms were found in the blood during the acute spreading stage of the disease.

NOTES ON THE INCIDENCE OF YEAST-LIKE ORGANISMS IN CHRONIC PARONYCHIA. D. H. HALER, Brit. J. Dermat. **43**:343 (July) 1931.

An investigation of the bacteriology of subacute and chronic paronychia was undertaken by the author, and the results of the examination of twenty-five cases are presented in a table, together with a detailed description of the common clinical picture, the technic of culture and the examination of ten controls. It was noted that a large percentage of the cases under consideration were in women, and that the disease is usually bilateral and in the majority affects the posterior nail-folds. There is no predilection for either hand or any particular digit. It is apparently limited to the posterior nail-folds and the tissue immediately subjacent. The nail is not affected. The formation of pus and lymphangitis are extremely rare. There are a peculiar red, raised, bolster-like appearance of the posterior nail-fold and a marked separation of the eponychial layer from the superior surface of the nails. Monilia were present in twenty-four of twenty-five clinically suspected cases. Other organisms, Staphylococcus aureus and albus, Micrococcus flavus and tetragenus, Streptococcus ignavus and faecalis, Sarcina lutea and sublutea, Bacillus proteus and Bacillus coli-aerogenes, were cultivated in widely varying numbers and differed in type and virulence from case to case.

CARCINOMA ERYSIPELATODES. C. RASCH, Brit. J. Dermat. **43**:351 (July) 1931.

A case of carcinoma erysipelatodes is described in an unmarried woman, aged 64, who, following a pin scratch in the left mammary region, subsequently noted a diffuse swelling in the area. Later the skin over the sternal and both mammary regions, with extension to the epigastric region and the left infraspinous area, was bright red to bluish red, diffusely thickened, stiff and nonpitting and could not be lifted up into folds. The skin felt warm and was only slightly tender. The edge of the affected area was irregularly wavy in outline.

only slightly raised above the level of the healthy skin and showed a flaring erysipelatous redness. With its clinical appearance, its rapid spread like that in erysipelas and its morbid anatomy with the intravascular growth of carcinoma cells, the disease presents a characteristic picture. It is to be distinguished from "cancer en cuirasse" by the lack of scleroderma-like condition, and by the fact that the cells in the latter type of carcinoma are found mainly in the lymph vessels and tissue spaces. A reproduction of a moulage and two photomicrographs illustrating the histologic picture accompany the article.

WIEN, Chicago.

THE ETIOLOGY OF DYSHIDROSIS. G. B. DOWLING, Brit. M. J. **1**:142 (Jan. 23) 1932.

Dowling believes that the conception of Tilbury Fox of disturbance of the innervation of the sweat glands must be abandoned, for it has been demonstrated that dyshidrosis is vesicular eczema. Most cases are due to ringworm infection. Exogenous irritants may produce a condition objectively identical with dyshidrosis of the hand, usually in those who suffer from hyperhidrosis of the palms and soles. Dyshidrosis may be a manifestation also of seborrheic eczema, or of eczema of any type such as varicose eczema or pruritus ani with eczematization, in which cases the lesions on the hand are due to sensitization of the skin, generally by the products of tissue autolysis derived from the primary foci. There is another type of idiopathic or true dyshidrosis, the type that recurs at intervals during the summer months. Patients with this condition invariably suffer from hyperhidrosis, and it is suggested that perhaps the sweat itself is the causal irritant; i. e., the patient is sensitive to his own sweat. The pertinent literature is briefly reviewed.

RATTNER, Chicago.

AN INVESTIGATION INTO THE PART PLAYED BY MATERNAL SYPHILIS IN THE CAUSATION OF FETAL AND INFANT DEATH AND THE EFFECTS OF ANTENATAL TREATMENT. E. J. PYE-SMITH, J. Obst. & Gynæc. Brit. Emp. **38**:578, 1931.

The author concludes from the careful study of his cases that maternal syphilis is not a common cause of abortion, either before or after the third month of pregnancy. It is, however, an important cause of stillbirth and of infant death from syphilis or intercurrent infections. Death is most frequent during the first six months of life. The treatment of the mother during pregnancy is of great benefit: The percentage of premature births is reduced, the percentage of live births is raised, and proportionately more infants whose mothers are treated than those whose mothers are not treated survive the first year of life. The results of the investigation indicate that the incidence of maternal syphilis in the author's locality is probably less than 2 per cent. He believes that abortion is not especially common among syphilitic women. Maternal syphilis causes the most harm in the later weeks of pregnancy and the first months of postnatal life, as stillbirths and infant deaths are much more frequent when the mother is the subject of syphilis. Good results follow treatment with neoarsphenamine, even when an efficient course cannot be given. The disease is not so common, the treatment is easily applied, and it is followed by a suppression of the more disastrous consequences of the disease.

ADAIR, Chicago. [AM. J. DIS. CHILD.]

A CASE OF POISONING FROM HAIR DYE. W. JOHN CLOSE, M. J. Australia **1**:53 (Jan. 9) 1932.

This is an interesting report of a case in which a woman complained for years of symptoms referable to the gastro-intestinal tract and the nervous system. She had had repeated attacks of nausea and colitis, headaches, giddiness and paresthesias, until finally she became bedridden. The toxin was found to be paraphenylen-

diamine contained in a hair dye that she had used at intervals for years. Apparently, it had never caused a cutaneous eruption, as there is no mention in the article of involvement of the skin. The preparation used was Inecto.

RATTNER, Chicago.

A STRIATED BULLOUS DERMATITIS DEVELOPING CONSECUTIVE TO SUNLIGHT BATHS. M. OPPENHEIM, Ann. de dermat. et syph. **3**:1 (Jan.) 1932.

In 1926, Oppenheim described a new dermatosis, and has since observed a number of cases. He calls it dermatitis bullosa striata pratensis, and the cause has not yet been found.

It develops in persons who have bathed in rivers or public baths and then exposed themselves to the sun on the beach. The eruption appears on the uncovered parts of the body after an incubation period of from twenty-four to forty-eight hours, and consists of red macules and striae on which lentil-sized bullae supervene. The lesions have a grouped arrangement, suggesting that of herpes, and by confluence may become as large as a chestnut. Itching is marked. The condition clears up promptly under mild local applications, leaving pigmentation at the borders of the lesions which persists for several months. The histologic picture is that of an acute vesicular dermatitis.

Whether the cause of the disorder lies in the baths, the earth, the sun or a vegetation, the author has been unable to prove. The condition acts like a sensitization dermatitis, perhaps due to plant life and perhaps also to other factors that do not manifest themselves except under favorable conditions.

INTERTRIGO OF THE TOES AND A NAIL INFECTION DUE TO A NEW PARASITE. L. BALINA and P. NEGRONI, Ann. de dermat. et syph. **3**:8 (Jan.) 1932.

The authors claim to have proved a new type of yeastlike organism, related to Verticillium, pathogenic for the nails and epidermis of man. Detailed mycologic and cytologic studies are set forth.

THE RADIUM TREATMENT OF CUTANEOUS EPITHELIOMAS. A. LASSNEUR, Ann. de dermat. et syph. **3**:21 (Jan.) 1932.

The fruitage of sixteen years of experimental work is here published in the form of a series of tables, which set forth in detail the various factors employed in the radium treatment of epitheliomas; they may be used as a guide by those who engage in this work.

GANDY, Houston, Texas.

DERMATOMYOSITIS. G. MARINESCU, S. DRAGANESCU and E. FAÇON, Ann. de méd. **30**:145 (July) 1931.

A chauffeur, aged 18, entered the hospital with complaints of pain, difficulty in the use of both the upper and the lower extremities and difficulty in swallowing. The left cheek, the nose, the eyebrows and the upper part of the face were swollen, red and painful to pressure. The outlines of the swollen parts were diffuse, with desquamation of the surrounding skin. There was difficulty in swallowing fluids; the speech was slow and nasal. Movements of the upper jaw and of the upper and lower extremities were carried out with difficulty; the muscular power was diminished. The muscles of the arms and hips were diffusely swollen, hard and painful to pressure. Tendon and cutaneous reflexes were normal; sensation was not disturbed. Electric examination of the muscles involved showed a quantitative diminution of reaction to faradic and galvanic stimulation. Histologic examination of a piece of muscle removed at biopsy showed an intensive interstitial inflammatory reaction, with degeneration of the muscle fibers.

The patient died after six months. Microscopic examination showed multiple inflammatory foci of the subcutaneous tissue, the interstitium and the parenchyma

of the different muscles involved. The cellular infiltration consisted mainly of lymphocytes, together with a marked proliferation of sarcolemma nuclei. In the peripheral nerves, isolated small foci of demyelinization were found, with isolated degenerated nerve fibers. The most prominent feature was the infiltration of small round cells in the perineurium and around the interstitial vessels. A similar picture was seen in the capsule of the spinal and sympathetic ganglions. In the dorsal spinal cord, minute lymphocytic cuffing around smaller veins of the lateral horns and the white matter were found.

"Poikilodermie myopathique" (type Petges-Cléjan) is closely related to dermatomyositis. The pigmentation of the skin in the first disease and the spreading of the inflammation to the corium are important points of differential diagnosis. Sclerodermia presents a histologic picture similar to dermatomyositis, but the chronic course and the typical cutaneous lesions characterize the first disease. In polyneuritis, cutaneous changes are absent. Kussmaul's disease is recognized by the periarteritis nodosa. Tuberculosis, rheumatism, angina, influenza, focal sepsis, etc., have been considered as etiologic factors. The authors think of a filtrable virus, similar to that which had been demonstrated in periarteritis nodosa, with a special affinity for connective tissue and vessels.

WEIN, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

OCULAR PEMPHIGUS AND SKIN GRAFTS. F. TERRIEN, GOUGEROT and HASSON, Arch. d'opht. **48**:275 (April) 1931.

The authors' case of classic cutaneous pemphigus, with predilection for the mucous membrane of the eyes and mouth, is especially interesting from the point of view of treatment. Although it is often thought that treatment is of no avail, recently suggested methods have yielded unhoped for results. These are autohemotherapy, sodium cacodylate and the arsenobenzenes and intramuscular injections of tartrobismuthate of sodium. More recently Spillman and Watim have recommended the subcutaneous injection of from 5 to 10 cc. of a 5 per cent Witte's peptone solution, 40 drops of epinephrine being given by mouth the first day, 0.2 Gm. of ergotin orally the second day and an intravenous injection of 5 cc. of a 10 per cent solution of calcium chloride the third day. The authors point out the necessity of having several modes of treatment available, as in some instances one form may aggravate the condition in one patient and another in others. The observation by the patient of the cessation of the cutaneous lesions following an attack of measles with high fever led the authors to use autohemotherapy to produce a temperature reaction, with success in their case.

The prevention of symblepharon in these cases is almost impossible. In the authors' case they successfully dissected the lids from the globe and introduced skin grafts. This resulted in greatly improved motility of the eyes and relief from pain and photophobia. A patient with a similar case was successfully operated on in 1928.

MARLOW, Syracuse, N. Y. [ARCH. OPHTH.]

PARAPSORIASIS EN GOUTTES (BROCQ). C. ADRIAN, Bull. Soc. franç. de dermat. et syph. (Réunion dermat. de Strasbourg) **38**:1414 (Dec.) 1931.

A typical case of guttate parapsoriasis is presented, and in the discussion Pautrier states that this condition is so rare in France that he has not had a case in his clinic for thirteen years, yet he found in America that five or six cases would be presented at a single society meeting.

GANDY, Houston, Texas.

PRECOCIOUS INTERSTITIAL KERATITIS. A. IANCOU, Nourrisson **19**:278 (Sept.) 1931.

Interstitial keratitis is one of the late manifestations of congenital syphilis. That it may occur in early infancy is shown by a review of the literature. The

author reports two additional cases occurring in girls aged 4 and 4½ months, respectively. In one case the keratitis developed while the baby was receiving antisyphilitic treatment with neoarsphenamine.

McClelland, Cleveland. [Am. J. Dis. Child.]

Modern Conception of Acrodynia. M. Pehu and H. Jarricot, Paris méd. **2**:390 (Nov. 7) 1931.

The clinical symptoms of acrodynia are hypotonia, adenopathy and pyrexia, and the spinal fluid usually shows an increase in albumin. At autopsy diffuse lesions are found both in the peripheral nervous system and in the mesocephalic region. These resemble somewhat the lesions of poliomyelitis. There are two possible causes: first, avitaminosis, but the fact that the disease lasts in such a chronic form and cannot be induced experimentally in the human being makes this theory doubtful; second, an intoxication, but this must be intrinsic or extrinsic. An external factor cannot be proved, but in favor of an intrinsic factor is the frequent association with nervous disorders. Acrodynia is occasionally associated with encephalitis, and the question arises whether it may not likewise follow influenza.

Some Conditions of Infancy Accompanied by Induration of the Skin. R. Fischl, Rev. franç. de pédiat. **7**:401 (April) 1931.

The author reviews the literature on scleroderma and sclerema, and reports five cases of his own to show that this condition is a terminal symptom in certain infectious and noninfectious conditions. The first case was in a boy, 3 months old, in whom the sclerema followed pneumonia and suppurative pleurisy; the second followed alimentary intoxication in a 5 months old girl; the third case occurred in a boy aged 1 month following meningitis; the fourth in a 6 months old boy following digestive disturbances, and the fifth in a 7 days old premature infant with atelectasis. Microscopically, the skin showed a necrosis of the subcutaneous fat cells; if there was any inflammation, it was shown by a microcellular infiltration, with some proliferation of fibroblasts at the base of the fat lobules that were necrosed. In cases of long duration there is a formation of calcareous deposits in the spaces between the subcutaneous fat cells.

Attempts to produce similar histologic pictures in the rat and rabbit by skin friction and ethyl chloride were unsuccessful, particularly in that there was no inflammatory reaction. To prove, however, that in the human being for the first six months the skin may present modifications of the aforementioned changes following infection, histologic examinations were made of seven infants under 7 months of age who died of various infections. The subcutaneous fat showed a number of variations from the so-called normal.

The conclusion is therefore drawn that in the infant there is a series of conditions accompanied by a cutaneous induration in which alteration of the subcutaneous fat cells plays an important rôle. The difference in type is due simply to transition. If the initial state is without inflammation, the reaction will be of short duration. These changes in the tissues may be of the utmost importance to the ultimate outcome of a generalized disease.

An Epidemic Disease in Infants Characterized by a Miliary Exanthem. A. Stroé, Rev. franç. de pédiat. **7**:467, 1931.

The author describes a disease that was epidemic in infants' hospitals in Bucharest in 1923, the symptoms of which do not fall into any of the accepted classes of exanthems. The incubation period was from six to fourteen days. The period of invasion was from two to five days. This was characterized by a temperature of from 38 to 39 C. (100.4 to 102.2 F.), an oculonasal catarrh and a redness of the tonsillar pillars. The exanthem consisted of small, rose red macules which tended to form plaques and on which small vesicles formed as a final stage.

These either were absorbed or ruptured, causing a desquamation. The desquamation was present on the face, body, extremities, palms and soles. The disease was contagious for two thirds of the children exposed. The blood showed a mononucleosis of 70 per cent, and there was sometimes an apparent increase of cerebral pressure. One case was considerably relieved by a spinal puncture. The spinal fluid was normal.

CYTOSTEATONECROSIS IN A CASE OF RITTER'S DISEASE. BELLOCQ, LAUTIER and MEYER, Rev. franç. de pédiat. **7**:489, 1931.

Pemphigus developed in an infant on the twelfth day of life, and death occurred on the twenty-fifth day. The skin showed histologically a diffuse infiltration of polymorphonuclears as an inflammation, with reabsorption of the fat cells. The fat contained in the adipose cells was separated into droplets. The characteristic picture is the inflammation of the vascular tissue, with absorption of the adipose tissue and replacement by connective tissue.

SANFORD, Chicago. [AM. J. DIS. CHILD.]

SIX YEARS OF MALARIA THERAPY IN GENERAL PARALYSIS. TANCREDI CORTESI, Rassegna di studi psichiat. **20**:770 (July-Aug.) 1931.

The author reports the results of his experience with malaria therapy from 1924 to 1930, and takes into consideration the period of incubation, the type of febrile reaction, the response to malaria, the sensitivity to quinine, the course and complication of malarial therapy, the mental manifestations during the febrile reaction and the result of the treatment. He also takes into consideration the antisyphilitic treatment administered to patients before the malaria.

The conclusions of his observations are that of seventy-six patients with dementia paralytica treated with malaria, 18.4 per cent showed complete remission, 14.4 per cent partial remission, 13.1 per cent slight remission and 26.2 per cent no improvement.

In comparing the results in patients treated with malaria with those in nontreated patients, the author points out that of forty persons with dementia paralytica admitted to the hospital from 1919 to 1924, thiry-three died during the following five years, thus making the percentage of death in nontreated patients 85, as compared with 26.8 per cent in those having received the malarial treatment.

NEURAXITIS FROM HERPES ZOSTER. CESARE BELLAVITIS, Riv. di neurol. **4**:337 (Aug.) 1931.

The author reports the case of a patient, aged 53, with dementia praecox, in whom herpes zoster developed in the territory of the left second, third and fourth cervical roots. A few days later, when the cutaneous manifestations were disappearing, a left facial paralysis developed and a few days later a left hemiparesis, accompanied by mental confusion. Five months later, the patient died: at autopsy a diffuse congestion of the cerebrospinal axis was found. Histologic examination of the cervical ganglions showed an inflammatory process extending to the corresponding spinal roots. However, the process was not limited to the roots and to the ganglions, but invaded the cervical segments of the spinal cord, where congestion and perivascular infiltration were found both in the white and in the gray matter. In the gray matter the nerve cells were considerably involved, especially those in the posterior horns. The process extended also into the pons, the basal ganglions and the cortex. The lesions there also were of an inflammatory nature.

The author upholds, therefore, the conception of a zoster myelitis as first described by Brissaud and recently carefully investigated by Lhermitte and his co-workers. The author's conception departs from the old conception of herpes zoster as a ganglioradiculitis, the cutaneous manifestations of which are of a dystrophic nature, and substitutes for it the conception that makes of the zoster a superficial manifestation of a generalized neurotropic infection.

A Case of Acrodynia (Infantile) of Selter-Swift-Feer in a Youth Aged 19. F. Pennacchi, Riv. di pat. nerv. **37**:126 (Jan.) 1931.

The author reports the case of a youth, aged 19, who previously had been normally developed both physically and mentally, and whose behavior gradually modified so that in a few weeks he became mute, indifferent and negativistic, and had incontinence of urine and obstinate constipation. Neurologically, there were some muscular atrophy of the hands and some hypertonus. There was considerable hyperhidrosis, involving particularly the head, hands and feet. The pupils were enlarged and sluggish in reaction. Saliva was abundant. Three months later, a trophic condition of the feet, represented by desquamation developed. The skin of the feet was cyanotic. Later, desquamation was noticeable also in the palms. In his attempts to walk, the patient disclosed great carefulness and slowness, and walked as if he had pain in the feet.

The author discusses the symptomatology and pathogenesis of the condition, and concludes that the case should be classified as acrodynia as described by the French author, Chardon, in 1828, described later by Selter in 1903 under the name of trophodermatoneurosis, eleven years later by Swift under the name of erythroedema and in 1921 by Feer under the name of neurosis sui generis of the vegetative system. Though the reports of cases in Europe, America and Australia deal essentially with the infantile form, the author believes that his case may belong to the group of acrodynia. The author believes also that from the pathogenic standpoint the condition is due to a virus infection similar to, but not identical with, that of epidemic encephalitis, which enters the body through infection of the rhinopharynx. The infection seems to have a predilection for the vegetative centers of the diencephalon and mesencephalon.

Ferraro, New York. [Arch. Neurol. & Psychiat.]

Unilateral Furred Tongue as Symptom of Trophic Disturbance: Relation of Trophicity and Function. J. Dawidow, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **130**:157 (Dec. 17) 1931.

Dawidow defines "normal Trophik," here translated "normal trophicity," as "that relation between assimilation and dissimilation which affords the biologically optimal state of nutrition and the specific structure of the functioning unit." He discusses the influence of the nervous system on trophicity, citing several clinical and experimental observations from the literature which show that peripheral trophic disturbances can result from injuries to the sympathetic nervous system as well as from injuries to the motor nervous mechanism. Contrary to the opinion of some authors, he thinks that trophic disturbances can also be caused solely by injuries to the sensory nerves. To support this view he reports several clinical cases from his own experience in which a lesion of the sensory trigeminal nerve resulted in a furred tongue. In four cases division of the trigeminal nerve because of neuralgia resulted in unilateral fur of the tongue. In the other two cases, the tongue became furred on one side following a bullet injury to the sensory trigeminal center in the cortex. The author feels that he has herewith refuted the opinion of some writers, that trophic disturbances in passive organs are due to injuries of special "trophic fibers" of the sympathetic nervous system and that such disturbances cannot be attributed to exclusive injury of the sensory fibers. Clinically, these cases are of interest as they show that a furred tongue, if the condition is pronounced and lasting, may point to an organic injury of the sensory trigeminal mechanism.

Editor's Abstract. [Arch. Otolaryng.]

The Morphology and Biology of the So-Called Schizosaccharomyces Hominis Benedek. O. Dittmann, Dermat. Wchnschr. **93**:1925 (Dec. 12) 1931.

As a result of a bacteriologic investigation of a strain of schizosaccharomyces hominis obtained from Benedek's laboratory, the author concludes that the organism is a bacterium. He finds that it is similar in most respects to Bacillus megatherium and agrees with Kruse in calling it Bacillus megatherium-hominis.

THE TREATMENT OF CHRONIC ALIMENTARY URTICARIA, ANGIONEUROTIC EDEMA AND DYSHIDROSIS (ECZEMA DYSHIDROTICUM) IN DAILY PRACTICE. JOSEF SELLEI, Dermat. Wchnschr. **93**:1963 (Dec. 19) 1931.

The author makes use of sugar-free diet, with a limited amount of flour. In addition, he prescribes calcium and intramuscular injections with a parathyroid extract, combining calcium therapy at times with generalized ultraviolet irradiation and the administration of atropine.

THE TREATMENT OF ERYSIPELOID WITH ACRIFLAVINE. WALTER K. FRÄNKEL, Dermat. Wchnschr. **93**:1967 (Dec. 19) 1931.

Fränkel advises painting the erysipeloid lesions thoroughly with a 3 per cent alcoholic solution of acriflavine, followed by a dressing of sulphonated bitumen N. F. This treatment is repeated every two days. The average number of treatments required was three, and the largest number used was six.

PERMANENT ALOPECIA FOLLOWING ROENTGEN EPILATION OF THE SCALP. CARL SPEIERER, Dermat. Wchnschr. **94**:1 (Jan. 2) 1932.

Permanent alopecia followed the roentgen epilation of a 6 year old girl for tinea tonsurans. A failure of technic was excluded. The same dose has been satisfactory in 401 cases in which treatment was used before and since this patient was treated. The age of the patient as a factor was excluded by the fact that 82 of the 401 patients ranged from 2 to 6 years of age. The author was told by the child's mother that her hair had not appeared until she was 2 years old, and he concludes that possibly a glandular dystrophy (parathyroid?) was responsible for a decrease of the power of regeneration of the hair.

THE TREATMENT OF CONGESTIVE CUTANEOUS CONDITIONS WITH THE ELASTOPLAST HALF-WIDTH BANDAGE. PAUL UNNA, JR., Dermat. Wchnschr. **94**: 3 (Jan. 2) 1932.

This bandage is elastic, and half its width is adhesive. It can thus be applied to the leg in such a way that, except for the first turn, the adhesive surface is not attached to the skin. Unna discusses its manifest advantages in the treatment of varicose eczema and ulcers.

ARSPHENAMINE PURPURA. HORST-GÜNTHER BODE, Dermat. Wchnschr. **94**:12 (Jan. 2); 54 (Jan. 9) 1932.

A patient with chronic lupus erythematosus and latent syphilis received a total of 0.9 Gm. of neosilver arsphenamine in the course of twelve days. A profuse hemorrhage of the gums, tonsils and nose occurred, with generalized purpura of the skin and mucous membranes and secondary anemia. Changes in the blood, such as aplastic anemia, did not occur. Changes in the skin and mucous membranes were the only toxic manifestations. The cause of the condition was probably an abnormal reaction of the drug in the walls of the blood vessels. The smallest amount of arsphenamine caused a recurrence of the purpura.

UNUSUAL FORMS OF ERYSIPELOID. WILHELM RICHTER, Dermat. Wchnschr. **94**:45 (Jan. 9) 1932.

A case of erysipeloid is described in which the eruption spread over the entire body. The diagnosis was verified by the recovery of the swine erysipelas bacillus (Bacillus murisepticus). Of special interest was the fact that there was a septic temperature with remissions in the evening. Specific antiserum was used successfully.

PAPILLOMATOUS TERTIARY SYPHILIS. J. SAMEK, Dermat. Wchnschr. **94**:50 (Jan. 9) 1932.

Four patients with papillomatous lesions were studied clinically and histologically by the author. The question arises as to whether these lesions are secondary to the syphilitic lesion or whether they are gummatous. Samek concludes from the histology that they are gummatous.

THE RELATIONSHIP BETWEEN TRAUMA AND PEMPHIGUS. RUDOLF M. BOHNSTEDT, Dermat. Wchnschr. **94**:89 (Jan. 16) 1932.

The author describes briefly six cases of pemphigus that followed surgical trauma. In three of them, the cutaneous eruption started in the region traumatized and followed shortly after the operation. In the three remaining cases the apparent connection was not close.

TAUSSIG, San Francisco.

AMBIGUITY OF BLEPHARITIS DIPHTHERITICA. FRIEDMAN, Deutsche med. Wchnschr. **57**:1542 (Sept. 4) 1931.

A child of 2½ years had exhibited a scrofulous inflammation of the lids for about two months. The mother gave a positive tuberculous history, but thorough examination of the child failed to reveal any evidence of tuberculosis. The margins of the lids, especially the upper lids, showed a picture of eczema, interrupted by greatly inflamed masses, which were moist. No membrane was present. The conjunctiva, nares and throat were normal. The temperature was also normal. A culture was reported negative after twenty-four hours, but was later positive for diphtheria bacillus. A maid at the patient's home had a mild, moist eczema involving the outer canthi of both eyes. She had been under treatment for about a year with no benefit. A culture demonstrated diphtheria bacillus. Both patients were cured by serum therapy, the child after eight days and the maid after two weeks. The author thinks that the organism was of the alternated variety.

L. L. MAYER. [ARCH. OPHTH.]

THE TRANSMISSION OF INGUINAL LYMPHOGRANULOMA TO RABBITS AND GUINEA-PIGS. H. FREUND and F. REISS, Klin. Wchnschr. **10**:1658, 1931.

In rabbits infected by the subdural inoculation of material from cases of inguinal lymphogranuloma, a characteristic meningeal encephalitis developed. Enlargement of the lymph nodes of the groins of rabbits was produced with material from man as well as with brain tissues from specifically diseased animals. These lymph glands had the characteristic histologic changes. Similar transmission experiments were successful in guinea-pigs. The infection can be transmitted from one animal species to another by inoculation.

[ARCH. PATH.]

THE TRANSMISSION OF INGUINAL LYMPHOGRANULOMA TO GUINEA-PIGS. K. MEYER, H. ROSENFELD and H. E. ANDERS, Klin. Wchnschr. **10**:1653, 1931.

The subcutaneous injection of exudate or crushed lymph gland tissues of patients with inguinal lymphogranuloma into guinea-pigs transmits the disease. Inoculations in ten cases were successful. The disease was transmitted from one guinea-pig to another, and in this way one virus strain was transplanted to the fifth and another to the twelfth generation. The virus passes through the Berkefeld filter and is markedly resistant to heat and the action of glycerin. The specific agent transmitted to the guinea-pig is not localized at the site inoculated, but spreads by way of the lymph channels and the blood. Systemic lesions occur in the liver and lungs. The diseased lymph nodes of the guinea-pigs are histologically the same as those of man.

AUTHORS' SUMMARY.

THE SENSATION OF ITCHING, SCRATCHING AND THE PILOMOTOR REFLEX IN INFANCY. D. H. KARPLUS, Jahrb. f. Kinderh. **132**:140 (July) 1931.

Of one hundred infants under 1 year of age, practically all in each age group reacted to the application of a commercial "itch-powder" to the skin by more or less varied bodily movements; it is assumed that they felt the itching. The most violent reactions were found at the sixth month. Scratching appeared at the third month. Pilomotor responses to various stimuli were noted at all ages. It is concluded that the striking difference between erythroderma in the first few months of life and true eczema thereafter cannot be attributed to any lack of nervous response by the skin early in life. An excellent discussion of the literature is included.

CLAUSEN, Rochester, N. Y. [AM. J. DIS. CHILD.]

TABES DORSALIS IN CONGENITAL SYPHILIS. M. NONNE, München. med. Wchnschr. **78**:632 (April 10) 1931.

Nonne reports two cases of congenital syphilis with tabes dorsalis. This is an infrequent combination. In one case Wassermann tests of the blood and spinal fluid on several occasions were negative. The second case was one of congenital syphilis in the third generation. An examination of the spinal fluid when the patient was 8 years of age showed a 3 plus Wassermann reaction and a paretic colloidal gold curve. Seven years later there was no paralysis (only slight mental retardation) and the tabes had not increased. The tabetic symptoms were absent; the achilles and patellar reflexes were obtained, and there was a diminished sensation of pain in both feet. Nonne warns against making a poor prognosis on the basis of the reaction of the spinal fluid, and emphasizes the slow and benign course of tabes in congenital syphilis. Crises, joint manifestations and ataxia are usually absent.

BRAHDY, Mount Vernon, N. Y. [AM. J. DIS. CHILD.]

AGRANULOCYTOSIS FOLLOWING TREATMENT WITH NEOARSPHENAMINE. E. ESSENFELD, München. med. Wchnschr. **78**:2034 (Nov. 27) 1931.

After reviewing the literature on agranulocytosis following antisyphilitic treatment with neoarsphenamine, Essenfeld gives the clinical histories of two cases from his own observation. In the first instance the agranulocytosis developed shortly before the end of the first series of injections of neoarsphenamine; in the second case it developed immediately after. In both patients icterus was absent, but a severe thrombopenia (without hemorrhagic diathesis) existed. In both cases the disease had a fatal outcome. The author is convinced that the agranulocytosis was caused by the treatment with neoarsphenamine and not by the syphilis

[J. A. M. A.]

PRIMARY RETOTHELIAL SARCOMA OF LYMPH NODES. F. ROULET, Virchows Arch. f. path. Anat. **277**:15, 1930.

The normal lymph node contains four types of differentiated cells of mesenchymal origin. These are the lymphocyte, the fibrocyte of the connective tissue framework, endothelium and the reticulum or retothelial cell. To the three previously recognized types of tumors primary in the lymph nodes, namely, the lymphosarcoma or lymphoblastoma, the fibrosarcoma or fibroblastoma, and the endothelioma or endothelioblastoma, must be added a fourth group only more recently recognized, the reticulum cell or retothelial sarcoma. Tumors of the last-named group are characterized histologically by proliferation of the reticulo-endothelial cells and by the formation of reticulum fibrils. The lymphocytes are compressed and atrophied by the proliferated retothelial tissue and become greatly reduced in number, finally disappearing almost completely. The reticulum fibrils form a dense network, which may undergo collagenous transformation. The capsule is uninvolved in the early stages. Clinically, the tumors are characterized by slow growth and by infrequency of metastasis. In the cases described, with one excep-

tion, the growth attacked the lymph nodes of the upper part of the body. The distribution was: cervical nodes, three cases; axillary nodes, two; mediastinal nodes, three, and inguinal nodes, one.

EXPERIMENTAL TUBERCULOSIS OF THE SKIN. S. S. VAIL, Virchows Arch. f. path. Anat. **277**:115, 1930.

In 108 experiments, tuberculous material was introduced into the skin of guinea-pigs, rabbits and monkeys. The material used consisted of cultures of the tubercle bacillus of different degrees of virulence, emulsions of human skin affected by lupus and emulsions of organs of infected guinea-pigs. The intradermal inoculation resulted in the production of a skin disease very similar in its histologic characteristics to human lupus. The tuberculous process became generalized comparatively late and ran a more chronic course than that which follows the usual modes of inoculation. The more prolonged course of the generalized infection was characterized by absence of caseation and by a tendency to productive inflammation and cicatrization.

THE COLOR OF THE SKIN AND EXPERIMENTAL TAR CANCER. T. SUZUKI, Virchows Arch. f. path. Anat. **277**:139, 1930.

The proportion of cancers that followed the application of tar to the skin was greater in white mice and rabbits than in black animals of the same species. In animals with skin of mixed colors, i. e., with black and white spots, tar cancers developed more frequently in the white spots than in the black ones. The author concludes that the color of the skin is an important predisposing factor in experimental tar cancer.

W. SAPHIR. [ARCH. PATH.]

HISTOLOGY OF COCCIDIOIDAL GRANULOMA. R. H. JAFFÉ, Virchows Arch. f. path. Anat. **278**:42, 1930.

Because the disease has thus far been limited to the western hemisphere, Jaffé presents a study of two cases of coccidioidal granuloma observed at the Cook County Hospital, Chicago. Localization of the organism, Cryptococcus (Coccidioides) immitis, is followed by the development of miliary epithelioid nodules that do not tend to coalesce with each other and are separated by a dense infiltration of plasma cells. The cyst develops and ripens within a giant cell at the center of the nodule. Rupture of the cyst is followed by destruction of the giant cell and by infiltration by leukocytes, transforming the epithelioid nodule into a miliary abscess. In the skin, the histologic character of the granulation tissue is soon disturbed by secondary infection. The development of the miliary nodules about the capillaries leads Jaffé to conclude that infection of the skin occurs by way of the blood stream. In the experimental lesions of guinea-pigs, the characteristic epithelioid or histiocytic reaction is absent, the lesions being purulent from the beginning.

SYPHILITIC ULCER OF THE STOMACH. G. L. DERMAN and M. A. KOPELOWITSCH, Virchows Arch. f. path. Anat. **278**:149, 1930.

For the clinician, syphilis of the stomach is not a rare disease. For the pathologist, it is extremely rare. The authors report an ulcerative lesion of the stomach that they believe to be syphilitic, and not merely a coincidental peptic ulcer in a person with syphilis. The patient, aged 31, died of lobar pneumonia following an acute hemorrhage of the stomach. Autopsy revealed, in addition to the pneumonia, syphilitic cirrhosis of the liver with multiple gummas and amyloid infiltration of the spleen and kidneys. In the prepyloric region of the stomach there was a saddle-shaped ulcer of the greater curvature. The floor of the ulcer, which was covered at the margins by a thin layer of mucosa, was formed by a greatly thickened submucosa with perivascular lymphocytic infiltration and obliterating endarteritis of the larger arteries. The granulomatous process extended down into the muscle coats.

NERVE FIBRILS IN SQUAMOUS CELL CARCINOMA. W. MARTYNOW, Virchows Arch. f. path. Anat. **278**:498, 1930.

This is a study of the distribution of nerve fibrils in fourteen epitheliomas of the upper lip, two of the penis and one each of the tongue and upper lip. The methylene blue (methylthionine chloride, U. S. P.) and the Golgi silver impregnation methods were used for the demonstration of the fibrils. Details of the methods used and a brief review of the findings of previous workers are given. Intercellular nerve fibrils are found in the epithelial cell nests of squamous cell carcinoma and bear the same relations to the cells as in normal squamous epithelium. They are new-formed, naked axis-cylinders. In the supporting stroma of the tumor, the nerve fibrils often form dense, tangled networks. Fibrils were observed in keratinized cancer pearls; here they revealed various degenerative changes. Nerve fibrils were increased in number in the epithelium at the margin of the neoplasm. Farther away from the tumor they were normal.

O. T. SCHULTZ. [ARCH. PATH.]

THE RÔLE OF THE SKIN IN THE PRODUCTION OF ANTIBODIES AGAINST SPIROCHAETA PALLIDA. F. PLAUT, Ztschr. f. Immunitätsforsch. u. exper. Therap. **71**:223, 1931.

Very small doses of nonvirulent, pure cultures of Spirochaeta pallida, injected subcutaneously or applied on scarified skin, stimulated the development of specific agglutinins and lysins, but no advantage was observed when these routes were compared with the intravenous. Extracts of skin from the areas into which the antigen had been injected did not contain agglutinins, indicating a lack of participation by the skin in the production of antibodies against spirochetes from cultures. Virulent spirochetes from testicular chancres did not produce agglutinins when injected intracutaneously and did not react in vitro with serums prepared against cultural spirochetes.

DAVIDSOHN [ARCH. PATH.]

THE PATHOLOGY AND TREATMENT OF HYPERHIDROSIS. ARTHUR SCHWEITZER, Borgyogyaszati Szemle **60**:192 (Dec. 21) 1931.

In cases of abnormal sweating due to disturbances of the peripheral nerves, irritation of the peripheral nerves supplying the regional sweat glands can be demonstrated. Reference is made to a case of precocious sweating in which the loss of water was so great as to weaken the patient to the point of incapacity; severance of the nerves leading to the regional sweat glands (Schweissnerven) stopped the hyperhidrosis.

Drugs acting peripherally, such as cinchophen and agaricin, are useful in some cases, but may produce toxic symptoms.

Camphoric acid acts centrally. Through its use in tuberculosis, its ability to diminish hyperhidrosis was discovered. Drugs acting through the circulation are calcium and from 10 to 20 per cent sodium chloride solution. Formaldehyde and tannic acid solution used externally produce temporary results only.

Among the laity a plant, Salvia officinalis, has been used and a preparation from this plant is considered an efficient antihydroticum by the author.

SCHORR, Chicago.

TREATMENT OF SCLERODERMA WITH PANCREAS. J. SELLEI, Orvosi hetil. **75**:13 (Jan. 3) 1931.

Raw pancreas, ground and mixed with soup or broth, was given daily. The amount for children ranged between 30 and 50 Gm. It was, as a rule, given from one to one and a half hours before breakfast. An hour later pepsin and hydrochloric acid were given in small doses. In the first stages of scleroderma, when there was no atrophy, good results were seen in from four to six months. No relapses were noted.

ZENTAY, St. Louis. [AM. J. DIS. CHILD.]

RADIOSENSIBILITY OF HUMAN LYMPHOSARCOMA. CARL KREBS and FANNY BUSCH, Acta radiol. **12**:395, 1931.

From experiments carried out with transplants of human lymphosarcoma into mice, the authors find that the lethal dose for the tumor cells is about two erythema doses, or approximately the same as that for mouse lymphosarcoma, compared with five or six erythema doses for mouse sarcoma and carcinoma.

WIEDER, Milwaukee.

ECZEMA SEBORRHOICUM: II. III. ECZEMA SEBORRHOICUM AND VITAMIN A. F. C. KUIPERS, Nederl. tijdschr. v. geneesk. **75**:1108 (March 7) 1931; 3439 (June 27), and 3688 (July 14) 1931.

Starting from the idea that vitamin A has a specific trophic influence on certain epithelia of mucous membranes, the influence of this vitamin on the young skin was studied. With the aid of the reaction of Carr and Price the existence of vitamin A in the vernix caseosa of new-born infants was determined. Of the 136 vernices, 78 gave a positive reaction. In fatty substances in the scales of children with eczema seborrhoicum, vitamin A could sometimes be demonstrated with the reaction of Carr and Price; in some instances this was impossible. The children with a positive reaction showed a tendency toward spontaneous recovery, whereas those without vitamin A showed no such tendency. It appeared, moreover, that the alkali reserve of the blood was correlated with the existence or nonexistence of vitamin A in the fatty substance of the skin. Children with alkalosis had no vitamin A. Scheer has already pointed out the alkalosis of children with eczema and the therapeutic effect of his hydrochloric acid milk. The author recommends a method for inducing the skin to absorb vitamin A. He used the Dutch preparation. In many cases the eczema was cured without further treatment within from seven to ten days. In refractory cases hydrochloric acid was added, and often led to a complete recovery.

An investigation of the vernix caseosa of 200 new-born children showed that 32 per cent of them had no vernix; in 17.5 per cent the vernix gave a negative reaction for vitamin A, in 12.5 per cent a weak positive reaction and in 38 per cent a strong positive reaction. It seemed that the feeding of the mother had little influence on the vitamin content of the child's vernix. The vernix caseosa of a uniovular twin showed a large difference in macroscopic appearance as well as in the amount of vitamin A. The author is of the opinion that the composition of the vernix is determined by the child and not by the composition of the mother's blood. Two prominent types of vernix could be distinguished: homogeneous and cloudy. A distinct relation was found between the amount of fat and vitamin A of the vernix and the microscopic condition (homogeneous or not). The vernix caseosa, therefore, must be regarded as an important product. A further detailed microscopic investigation of the dried vernix showed that with the exception of the outer layer, the cells of the homogeneous vernix are round or oval, and that between the cells there is much fat. The cloudy vernix consists of flat cells showing keratosis for the greater part and lying close to each other; between the cells the amount of fat is small. The aforementioned difference in the structure of the vernix caseosa might point to a difference in the functional condition of the skin. The vernix thus could indicate the degree of keratosis during the later months of pregnancy, and the outer layer of the vernix could represent the condition of the skin at birth. This condition would be of great value in determining whether eczema seborrhoicum develops in the child. A number of children whose vernix had been studied at birth were therefore investigated after the age of 3 months. It was found that when there had been no vernix at birth, eczema seborrhoicum appeared in only 7 per cent. When the vernix at birth had been cloudy, i. e., contained little fat, a small quantity of vitamin A and cells showing much keratosis, the chance of developing eczema seborrhoicum was also small (12 per cent); when, however, the vernix was homogeneous the eczema seborrhoicum appeared in 42 per cent.

VAN CREVELD, Amsterdam, Holland. [AM. J. DIS. CHILD.]

Obituary

KEIZO DOHI, M.D.

1866-1931

A reprint has been received from the *Japanese Journal of Dermatology and Urology* (**31**: I [Nov.] 1931) of a tribute to Dr. Keizo Dohi, who was born in 1866 and who died Nov. 5, 1931. This tribute is another evidence that the Orient does some things better than we do. There is a handsome portrait of Professor Dohi, and then there are four pictures illustrating events in the funeral ceremony in his honor. The first shows the foreground of the hall, Aoyama Saijō, decorated for the farewell service; the second, incense-burning by Buddhistic Archbishop Rev. Michishige; the third, Mrs. Dohi burning incense in course of chanting the service, and the fourth, the crowd of attendants at the farewell service. Then follows an extensive sketch of Dohi's life in Japanese and shorter sketches in German, French and English. The whole is exquisitely done, with moving sentiment and in perfect taste. It is a worthy tribute to a great man who was a pioneer in dermatology in the far East. Dohi had an elaborate and thorough European training in general medicine and in dermatology in preparation for the chair of dermatology and syphilology in the Imperial University of Tokyo. He was first appointed assistant professor and, in 1898, professor of dermatology and syphilology. In 1926, in his 60th year, he retired from his position at the university, and was appointed honorary professor. In the meantime, during his active incumbency of the position, he became one of the leading figures in medicine in Japan, and one of its most important representatives in dermatology. He was showered with honors by the Japanese and other governments, and his achievements were recognized by honorary memberships throughout the world. He was not only famous as a physician, but well known as a Chinese poet, under the pen name of "Gakuken." Altogether, he was a great man whose loss we mourn.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, Oct. 21, 1931

MICHAEL H. EBERT, M.D., *Vice President, Presiding*

MULTIPLE BENIGN EPITHELIOMA OF THE SCALP. Presented by DR. A. W. STILLIANS.

An American woman of Polish descent, aged 42, first noticed growths on the scalp eighteen years before presentation. Since then they had slowly increased in number and size. Within the last few years they had appeared in small numbers on the trunk; later many small papules had appeared on the face. There was slight tenderness at times, which increased after injury to the tumors.

Intense roentgenotherapy had been given over the left frontal region, leaving a large scar with a small central ulcer, still open, although the last irradiation had been given in May, 1931.

The top of the scalp was thickly covered with more or less pedunculated tumors, red because of telangiectases on their surfaces, ranging in size from a few millimeters to over 2 cm. in diameter and elevated as much as 1.5 cm. Some of the tumors were sessile, others more or less pedunculated. The small growths were the color of the skin or pale pink and soft; the large growths were firm but not hard. There were many tiny papules closely set on the inner part of the brows. The area that had received roentgenotherapy showed scarring, with a number of flat nodules and a central ulcer, 0.5 cm. in diameter.

Histologically, the tumors were basal cell epitheliomas, with cysts here and there.

DISCUSSION

DR. OLIVER S. ORMSBY: I am pleased to see this case because it recalls cases that many years ago caused much controversy. They have been described under the title of endothelioma capitis, through the first case was recorded as "withering sarcoma of the scalp." There has been discussion as to whether or not the condition is basal cell epithelioma. In Adamsen's study of the subject, he concluded that the minority of the growths may have been sarcomas, but the majority were histologically basal cell epitheliomas. Notwithstanding the fact that the condition has been recognized for many years, this is the first case, I think, that has been shown in Chicago.

DR. HAMILTON MONTGOMERY: The case clinically corresponds to those described by Spiegler as endothelioma capitis. Whereas this condition was originally thought to be an endothelioma, more recent investigators have shown that it is usually a true basal cell tumor. It is important, however, to recognize that the lesions as a rule are relatively benign as compared with the usual basal cell epithelioma. The condition is more comparable in its degree of malignancy to epithelioma adenoides cysticum of Brooke.

DR. CLARK W. FINNERUD: Several years ago a somewhat similar case was seen at the Presbyterian Hospital. The history showed that four or five members of the family in two or three generations had had the infection. Metastases formed in the instance of the mother of two children who had it, and because of the histology, there being present basal cell-like nests containing colloid-like substance, a diagnosis of carcinoma metastatic from the thyroid was made. From the standpoint of the general pathologist, that seemed a logical interpretation. If you examine the section under high power magnification, you readily see the

colloid-like material in the nests of proliferated cells; this material makes the diagnosis definite.

DR. MICHAEL H. EBERT: In a case reported by Watnabe, a Japanese observer, lesions of cylindroma of the scalp were associated with lesions of the type of Brooke's multiple benign cystic epithelioma of the face. I believe that in this case we have the same combination.

DR. CLEVELAND J. WHITE: I wish to ask Dr. Montgomery whether he has recently seen the cases of endothelioma that were described by Busman. It would be interesting to know whether the histology of those cases was similar to this case.

DR. HAMILTON MONTGOMERY: The cases reported by Busman under the title of "malignant endotheliomas with cutaneous involvement" presented a different clinical and histologic picture than does Dr. Stillians' case. Gans classifies Spiegler's endothelioma capitis and cylindromas of the skin under the title "nevus epithelioma cylindromatosus."

DR. OLIVER S. ORMSBY: The English were as familiar with basal cell epithelioma of the usual type, and they gave much study to this particular tumor of the scalp. These cases do not resemble clinically the common basal cell epithelioma or rodent ulcer, but they have the same histology and origin. My point is that this case is classic endothelioma capitis.

POIKILODERMA ATROPHICANS VASCULARE (JACOBI)? Presented by DR. HAMILTON MONTGOMERY and DR. PAUL A. O'LEARY.

A Jewish man, aged 46, was first examined in the Mayo Clinic in June, 1931, for a cutaneous condition of five years' duration which started as a generalized erythema with superficial scaling. Exposure to cold increased the erythema and made motion painful. One year after onset the patient noticed the appearance of keratosic lesions on the soles and a spotted pigmentation associated with "wrinkling" of the entire skin. No history of muscular weakness or internal medication was obtainable, and he had received no treatment for the dermatosis. His general health had always been good. Until ten months before presentation he worked with scrap iron; since then he has worked in a gasoline and oil station.

Examination revealed an obese man with marked enlargement of the breasts. The skin of the entire body, except the mucous membranes, eyelids and fingers, was involved in a varying degree. There were patches of atrophy with fine wrinkling of the skin in addition to some lichenified plaques and areas of telangiectasia. A marked pigmentation of the skin, assuming a retiform arrangement, was noted in certain areas, between which were interspersed areas of atrophy and telangiectasia. Follicular changes were seen only in a small area on the back. In addition, a few erythema multiforme-like papules were noted on the knees; the color could be expressed from these papules by pressure. No pain or muscular atrophy could be demonstrated.

A general examination revealed the following noteworthy facts: a roentgenogram of the pituitary gland showed a calcified pineal gland, calcification of the falx cerebri and a small area of calcification in the internal carotid region. Blood studies, including differential and platelet counts, and coagulation and bleeding time were all within normal limits. There were several infected teeth and slight evidence of tonsillar sepsis. The basal metabolic rate was —9. Capillary studies by Dr. George E. Brown revealed changes that were different from those seen in the usual vascular disturbances or in scleroderma. The patient's sweat activity was reduced, but there was no increase in temperature on hot days. There was no evidence of sclerodactylia or of changes in the nails.

Specimens for biopsy were taken from an atrophic area, from a telangiectatic area on the abdomen and from a hyperkeratosic lesion on the right foot. Both of the specimens from the abdomen showed a similar histopathologic picture. The histopathologic picture resembled that of subacute disseminate lupus erythematosus, although the clinical features did not warrant such a diagnosis. There was

marked liquefaction necrosis of the basal cell layer, a lymphocytic infiltrate varying in amount and limited chiefly to the upper cutis and numerous chromatophores laden with melanin pigment. The infiltrate, however, was diffuse rather than perivascular in type. The elastic tissue was diminished to absent where the infiltration was occurring. Stains for hemosiderin were negative. In several areas there was marked atrophy of the epidermis but with preservation of the stratum corneum and stratum granulosum. Small amounts of mucin were present in the upper cutis. The sections from the foot presented a similar picture except for marked hyperkeratosis, moderate acanthosis with spongiositis and a relative lack of deposit of pigment in the cutis.

Clinical photographs, drawings of the capillary changes and microscopic sections were shown. Since the patient left the clinic he had been receiving thyrocal by mouth but without benefit.

DISCUSSION

DR. OTTO H. FOERSTER: There are points of approach to a diagnosis of this case in the pituitary changes that are present. Though there is an absence of myositis and rheumatic symptoms, such as were present in cases described recently in which pituitary changes were a feature in connection with the cutaneous alteration, the rapid development of a diffuse scaling process involving a large part of the cutaneous surface with subsequent atrophic changes and the development of a peculiar hyperpigmentation and punctiform telangiectasia, with areas of depigmentation, oblige us to give consideration to a diagnosis of poikiloderma atrophicans vasculare. However, many of the cases so diagnosed and recorded have been shown eventually to be variants of erythematous lupus, perhaps atrophodermas or the end-changes in scleroderma, and some later have been proved to be mycosis fungoides, while others have run the course of dermatomyositis. We have, therefore, a peculiar and complex clinical picture to interpret; just what may be rightly included in poikiloderma is difficult to state at the present time. I think the patient presents symptoms that will justify our considering the case as belonging to the group associated with changes in the pituitary glands. Dr. Montgomery told me that the histologic changes will rule out erythematous lupus and scleroderma with atrophy and that mucin is present. The presence of mucin is of especial interest in connection with recently reported cases in which mucin was found not only in the diseased skin but also in the macroscopically normal skin.

DR. E. P. ZEISLER: I wish to ask Dr. Montgomery what type of adiposity this patient has, pituitary or hypothyroid, and whether the cutaneous condition may not have something to do with an underlying endocrine disturbance. My impression is that it is a case of poikiloderma.

DR. DAVID LIEBERTHAL: I have no diagnosis to offer, but I wish to state that I saw the patient about three years ago. At that time he presented large erythematous patches with slight scaling, but there was no pigmentation or atrophy noted.

DR. OLIVER S. ORMSBY: I think it is by comparison of patients with unusual symptoms whom we have seen before that we are able to distinguish new entities. I think that this patient presents symptoms much like those of two other persons, one of whom was previously presented here, whose condition has not as yet been definitely classified. This patient, a woman, was first presented by me several years ago; she had hyperpigmentation, atrophy and telangiectasia resembling poikiloderma, but did not have that disorder. Professor Bloch and Professor Jadassohn saw her at different times and both men expressed the opinion that the condition was difficult to diagnose. The other patient was a man who presented a similar group of symptoms that I have studied privately.

My first case of poikiloderma showed several patches having the appearance of healed radiodermatitis, and the case has become so fixed in my mind that if I do not see patches like those of healed radiodermatitis I think the condition is not poikiloderma. On the other hand, many cases reported have resembled

different conditions, including lupus erythematosus and lichen planus. We do not know as yet what poikiloderma will include. I feel that the patient presented today and the two I have mentioned all show symptoms so nearly alike as to warrant further study in order to obtain a correct diagnosis.

DR. HAMILTON MONTGOMERY: The adiposity in this case is probably due to a dysfunction of the pituitary gland. The basal metabolic rate was —9. The amount of mucin present in the sections taken for biopsy was greater than that seen in the normal skin but not so marked as is seen in solid edema in extremities following exophthalmic goiter, as described by Dr. O'Leary.

The case was presented as probably poikiloderma atrophicans vasculare although I recognized the fact that there were many atypical features; in fact, there has been a divergence of opinion among other dermatologists who have seen the patient as to just how to diagnose the condition. The histologic sections in a measure simulate those of lupus erythematosus, whereas there were other changes not seen in that disease. Clinically, the condition could not be correlated with that of lupus erythematosus. Gans and others pointed out the similarity between the histopathologic picture of poikíloderma and lupus erythematosus and emphasized the occasional difficulty in differentiating between the two conditions. The patient showed no disturbance of the muscles and no true sclerodermatous changes. Acrodermatitis chronica atrophicans, I believe, can be ruled out by the absence of any "Grenze" (borderline) zone between the epidermis and the infiltrate. There was no history of exposure to drugs or of an occupational dermatosis such as war melanosis of Rhiel.

SUBCUTANEOUS NODULAR SYPHILID? Presented by DR. J. FRANK WAUGH.

A farmer, aged 23, had always enjoyed good health until the onset of his present trouble five years before presentation. There was no history of arthritis, painful joints or syphilis, and the Wassermann test was negative. The Wassermann tests of the patient's father and mother were negative.

The lesions were limited to the hands and feet and consisted of firm, nonpainful subcutaneous nodules, varying in size from that of a pea to that of a hazelnut. There were about one dozen nodules on the palmar surface of the fingers and thumbs and a few similar lesions on the heels and toes, most of which were between the joints. The overlying skin was normal in appearance. The nodules had never been painful and did not disappear spontaneously.

Histologic examination revealed chronic granulomatous inflammation.

DISCUSSION

DR. CLARK W. FINNERUD: I think the condition is an instance, judging from the section, of juxta-articular nodules not due to syphilis. Dr. Waugh told Dr. Ormsby and me about the case the other day and said the Wassermann reaction was negative. I suggested that he make a therapeutic test anyway, because from his description the case was so much like one of Dr. Ormsby's which proved to be of syphilitic origin. The sections from that case were somewhat different from those presented today. Dr. Michelson recently had a case, the sections of which were similar to Dr. Ormsby's. The distinctive thing about the difference of the two types is that in the syphilitic cases there occur sharply defined, dense nests of cellular infiltration, composed almost solely of lymphocytes, around the blood vessels, and the coats of the blood vessels are proliferated as seen characteristically in that disease. The marked changes in the connective tissue of the two types are indistinguishable. I believe Dr. Montgomery has seen several cases at Rochester, and I should like to hear from him.

DR. HAMILTON MONTGOMERY: Dr. Brunsting reported three cases, all of which showed definite clinical evidence of syphilis and responded quickly to antisyphilitic therapy. I showed the specimens taken for biopsy from two of the patients to Dr. Warthin, who was unwilling to make a diagnosis of syphilis on the basis of the histopathologic observations. This unwillingness simply emphasizes to

me that the histopathologic changes in juxta-articular nodes do not, as a rule, present a syphilitic picture. In a recent article by Hopkins in the *Bulletin of the Johns Hopkins Hospital,* a series of cases of juxta-articular nodes of both the rheumatic and syphilitic types were reported. The histopathologic changes were similar in both types. The rheumatic type, however, did not respond to anti-syphilitic therapy.

DR. MICHAEL H. EBERT: In the only two cases of this disorder that I have seen nodes were formed, and they were not so flabby. I should like to know whether the nodes in Dr. Montgomery's cases were firm or flabby.

DR. HAMILTON MONTGOMERY: The firmness of the nodules varies greatly in different cases. In one case the question was raised of a possible xanthoma. In one of our cases and in some reported in the literature there has been evidence histologically of some xanthoma-like cells. This would account clinically for the variation in the consistency of the lesions.

DR. E. P. ZEISLER: About one and a half years ago I presented a patient with subcutaneous fibroid nodules in the palms and buttocks. He gave a positive Wassermann reaction, and it was amazing to see how readily those lesions disappeared under antisyphilitic therapy.

DR. J. FRANK WAUGH: The case has been quite interesting to me, especially since, in the recent literature, there have been several cases of these juxta-articular lesions reported. One of the last reports was in the *Bulletin of the Johns Hopkins Hospital,* as pointed out by Dr. Montgomery. There were fourteen cases, twelve of which were due to syphilis and all of which cleared up under anti-syphilitic therapy. It might be of interest to you to hear what Dr. Hektoen and Dr. Moore said in regard to the histology of this case. They are greatly interested in it and admit that it is unusual. I showed them the photographs of the hands and feet; in that way they were fortified in studying the case. They made the following report:

"In the sections are several irregularly shaped areas of necrosis surrounded by inflammatory cells of the endothelioid type. The walls of the vessels of the surrounding tissue and the edges of the necrotic areas are thickened and have a perivascular round cell infiltration.

"The process is that of chronic granulomatous inflammation rather than that of tumor. It does not appear to concern endothelioma or any other kind of neoplasm in the strict sense, but it does concern a chronic inflammatory process with the production of fibrous tissue in which are irregular areas of necrosis with wavy margins. There are also occasional minute, cellular areas in which may be multinuclear but imperfect giant cells. In the larger areas of necrosis one sometimes sees amorphous or granular material.

"The areas of necrosis to some extent resemble gummas. A question was raised in the first report, but it has not been answered. On account of their location and structure, assuming the other nodules to be like the one now under examination, the nodules in this case recall those sometimes seen in connection with arthritic nodes. In any event, the case is unusual."

The patient has no arthritic or rheumatic history involving the small joints. The first time I saw him at the office I prescribed pot assium iodide, a dosage of 15 grains (0.972 Gm.) three times a day, which was increased to 25 grains (1.62 Gm.) with no apparent effect, and Dr. Potter gave several roentgen treatments, also without benefit. We will give some arsphenamine and see if there is any effect. I will try to report later.

PEMPHIGUS CHRONICUS: LIMITED TO MUCOUS MEMBRANES OF MOUTH, THROAT AND LEFT EYE. Presented by DR. B. B. BEESON.

A woman, aged 52, presented a disorder of four years' duration. Her original complaint was dysphagia and sore mouth, with rapid loss of weight. She had recurring attacks of blebs in the mouth, throat and left eye, and showed no improvement until about six months ago. There had been no formation of blebs

during the past six months. There was an adhesion between the eyeball and the lower left lid. She had gained 18 pounds (8.2 Kg.).

This patient was first presented before the society two years ago.

DISCUSSION

DR. CLARK W. FINNERUD: I think this was a very interesting case and wish to know whether a specimen of blood has been sent to Dr. Pels for examination.

DR. B. BARKER BEESON: I lost track of the patient for some time, so that this examination has not been made, but I intend to have it made at the first opportunity. There have been no cutaneous lesions at any time in this case. When the patient was shown about two years ago, she presented several blebs over the hard palate, and there was marked inflammation. At the same time there was a pterygium-like patch. Both of these conditions have recurred. A culture was made from the blood and stool, and both showed the same type of a streptococcus organism. A vaccine was made from this and has been given to the patient by her physician. I do not know whether or not there is a remission, but she is much better at present.

DR. OLIVER S. ORMSBY: From the clinical standpoint, I do not see how a diagnosis of pemphigus can be considered in this case. I have seen several cases of lesions limited to the eye classed by oculists as pemphigus. These must be different from cutaneous pemphigus, which is, as a rule, a fatal disorder. When pemphigus begins in the mouth, it usually runs a rapidly fatal course, though I have seen cases in which several months intervened before cutaneous lesions developed. It is conceivable that this patient may have had pemphigus of the mucous membranes for two years without other symptoms and without appreciable effect on the general condition, but it is not likely.

DR. B. BARKER BEESON: In looking up the literature one finds a number of cases in which patients have had lesions of the mucous membrane for several years and after perhaps five years or longer lesions have developed on the skin.

DR. OTTO H. FOERSTER: I agree with Dr. Ormsby, that these cases with benign lesions of the mucous membrane are not of the type in which cutaneous lesions eventually develop.

DR. HAMILTON MONTGOMERY: I am in entire accord with what Dr. Foerster and Dr. Ormsby have just said. I wish to report a case, however, of true pemphigus that first showed lesions of the conjunctiva, then lesions of the mucous membrane of the mouth and, finally, lesions of the skin. The patient died within a year.

DR. EDWARD A. OLIVER: I saw this patient when she was shown here at a previous meeting and said then that if the condition was real pemphigus involving the mucous membrane a fatal issue would ensue very shortly. We have watched pemphigus at the county hospital over a period of years, and every one who has shown lesions of the mucous membrane has succumbed to the disease very promptly. I know that these cases have been presented as pemphigus, but I cannot see how they can be classified as such.

DR. OLIVER S. ORMSBY: The particular cases that I referred to as being entirely unlike pemphigus as we know the disease are those limited to the ocular membrane.

DR. B. BARKER BEESON: This patient was seen at the onset of the malady by four otolaryngologists, and three of them diagnosed syphilis. The mouth was first affected; the ocular lesions appeared later. I shall be glad to send a specimen of blood to Dr. Pels and will report later.

BLACK HAIRY TONGUE. Presented by DR. E. P. LIEBERTHAL.

J. W., aged 71, presented himself at Michael Reese Dispensary, on Oct. 20, 1931, complaining of a growth of one year's duration on the dorsum of the tongue.

The lesion consisted of a fairly sharply defined hypertrophy of the filiform papillae, the size of a quarter, localized in the middle of the dorsum of the tongue, varying in color from a dark brown at the center to a light brown at the periphery, where a distinct hyperkeratosis was clearly visible.

DISCUSSION

DR. F. E. SENEAR: I should like to know whether any bacteriologic investigations have been made in this case. It seems to me that people are becoming more conscious of what they have in their mouths, for we see many more cases of hairy tongue than formerly. There have been varied reports as to their etiology, and I have been interested in this. You will recall Dr. Engman's article, in which he reported one case where he recovered a pure culture of pneumococcus, and another case appeared in the German literature at about the same time. This seems to have been lost sight of in the consideration of the possibility of fungous origin. Dr. Engman used a saturated solution of ox gall in his case, and I have used this solution in several of the cases I have seen. Some have shown the fungi, but none has shown the pneumococcus. Nevertheless, I have had good results. Some patients have been treated with gentian violet rays, with no effect. I should like to know if any of the other doctors have had any experience with this treatment.

DR. EUGENE P. LIEBERTHAL: The patient presented himself too late to make bacteriologic examinations. These will be made and reported at a later date.

DR. HAMILTON MONTGOMERY: With Dr. Thompson, I reported two cases of hairy tongue in which the organism on culture was found to belong to the genus Actinomyces and to differ relatively slightly from the organism found by Weidman. We have had unsatisfactory results with gentian violet ray. I am exceedingly grateful for the suggestion concerning ox gall.

ULCER (TUBERCULOUS) OF THE LIP. Presented by DR. A. W. STILLIANS.

An American woman clerk, aged 28, who had had pulmonary tuberculosis for over five years, noticed two and a half years ago an ulcer on the inner side of the left cheek. This was treated with radium and healed promptly. Soon afterward a second ulcer appeared on the inner side of the lower lip and persisted in spite of two treatments with radium. It caused pain only at times, chiefly during meals. The sputum had been free from bacilli for the past three months, and the patient had recently gained weight.

On the inner side of the left lower lip, about opposite the second left incisor tooth, was a triangular ulcer about 1 cm. on each side and about 0.2 cm. deep, with steep sides and an uneven base with necrotic material on it.

DISCUSSION

DR. E. P. ZEISLER: The lesion looks like an erosion, but when you palpate it there is a deep, nodular infiltrate. This is the localized nonmiliary type of tuberculosis of the mucous membrane described by Jadassohn and is very difficult clinically to differentiate from chancre and epithelioma. A biopsy is essential. I should be interested to know how Dr. Stillians proposes to treat the lesion. Electrodesiccation should be considered.

DR. F. E. SENEAR: I am glad to see this case because I have had two experiences with tuberculosis of the mucous membrane which brought out the point Dr. Zeisler has just made. The first I saw with Dr. Pusey. There was a lesion on the tip of the tongue which we both took to be chancre, but after several negative dark-field examinations we began to look further and found it to be tuberculosis of the mucous membrane. The second patient I saw last summer, a man, aged 60; I thought his lesion was a gumma of the tongue. He had a dense nodule with a fissure in the center which was ulcerated. Dr. Oliver was with me and agreed with the diagnosis. In my absence Dr. Nomland saw the patient and was convinced that he had carcinoma of the tongue. When I came back we

gave him a therapeutic test with mercury and iodides and later with bismuth, without any effect. We then took a specimen for biopsy, which proved the condition to be tuberculous. On going back into the man's history we found that he had an old fibrous, pulmonary tuberculosis years before. He was sent back to the referring physician, who found this condition had recurred. It was necessary to send the patient to Arizona.

DR. CLEVELAND J. WHITE: In several cases of tuberculosis of the mucous membranes I have seen that a previous history of tuberculosis may or may not be obtained. In one case of tuberculosis of the mucous membrane which was shown last year at one of our meetings biopsy showed typical tuberculosis. The boy had no physical or active evidence of pulmonary involvement. Under the water-cooled lamp, the lesions completely healed. That case was of about fourteen months' duration, according to his history.

DR. OTTO H. FOERSTER: It seems to me that the lesions this patient presented today are not those on which we can base a diagnosis of tuberculosis. The present symptoms are probably due to therapy. The classic ulcer of the mucous membrane in tuberculosis is the result of necrosis of closely set miliary foci and has a serrated or polycyclic border, the serrations representing the arcs of the individual necrotic foci. The ulcer is characterized by extreme pain. There is no mucous membrane lesion that I know of that is as painful as the tuberculous ulcer.

DR. ARTHUR W. STILLIANS: I apologize for presenting this patient with the clinical appearance so changed by treatment. When I told her to come in this reaction had not developed. Before, when the mucous membrane was at rest, there was a fissure. When the lip was stretched, it became a triangular ulcer with an uneven base.

DERMATITIS DUE TO "TRICHO" METHOD. Presented by DR. EDWARD A. OLIVER.

A white woman, aged 24, five years before presentation had been treated by the "Tricho" method for removal of superfluous hair on both arms and legs. At that time she was planning a career in the movies as a dancer and decided to have this hair removed. She did not remember the exact number of treatments she received but believed that she had about two treatments a week for a year.

Both arms, from the wrists to the shoulders and both legs from the ankles to the groins showed a sclerodermatous condition of the skin, with most marked telangiectasia; there was one ulcer in the left groin and another in the right popliteal space.

DISCUSSION

DR. EDWARD A. OLIVER: This young woman tells me that the "Tricho" system is no longer operating in Los Angeles. So many suits were brought against the company that it was forced to close. This is the third case of dermatitis due to "Tricho" treatments that I have had. The patient has an ulcer in the left groin and another in the popliteal space that I believe should be excised. We shall have a hard time getting suitable skin for a graft, I fear.

DERMATITIS DUE TO NICKEL-PLATED HAIR CURLERS (DEMONSTRATION WITH PHOTOGRAPH AND CURLERS). Presented by DR. JAMES H. MITCHELL.

A woman, aged 70, had typical lichen simplex chronica in the occipital region of thirty years' duration. She had used nickel-plated hair curlers every night during the thirty years. The dermatitis cleared and had remained clear for three months with the simplest treatment after she ceased using the curlers.

A letter from the manufacturer stated that the curlers were nickel-plated.

DISCUSSION

DR. JAMES H. MITCHELL: This case is interesting in view of the fact that so much has been said and written about neurodermatitis and what constitutes it.

If we look carefully enough for some local cause we are likely to find something. In some cases it is mycotic, and in many cases there is an external irritant. This condition, I think, is a clear case of nickel dermatitis. The patient tells me that she has used the same hair curlers for thirty years, and one of them certainly looks it. I wrote to the manufacturer, who told me frankly that the curlers are nickel-plated.

DERMATOLOGICAL CONFERENCE OF THE MISSISSIPPI VALLEY

Fifth Annual Session, New Orleans, Nov. 18, 1931

M. T. VAN STUDDIFORD, M.D., *Presiding*

HERPES ZOSTER; PYODERMA, ACUTE. Presented by DR. T. A. MAXWELL, New Orleans.

P. S., a white woman, aged 50, stated that for the two weeks before presentation she had suffered from pain in the thigh and sacrum. This was followed by a vesiculopustular eruption grouped in a linear strip over the left thigh and extending to the upper third part of the leg.

DISCUSSION

DR. OLIVER S. ORMSBY, Chicago: The patient had lesions that resembled herpes zoster on one side. There is a point I wish to emphasize about zoster that I have found to be of diagnostic value. True herpes zoster always has, in the early stages, an associated glandular involvement which is an important corroborative symptom. For example, when there is a localized herpetic eruption not typical of zoster situated on the foot, leg or elsewhere, if an accompanying painful gland is found, it would aid materially in diagnosis. Zoster due to arsenic does not have this glandular involvement.

I think that the patient has zoster, but that there is a secondary pyodermic infection that has masked its characteristics.

Furthermore, zoster does not always present a characteristic or typical eruption. We showed a patient before the Chicago Dermatological Society some time ago with a distribution of zoster and lichen planus-like lesions which on histologic examination proved to be zoster.

ALOPECIA OF THE LOWER LEFT EYELID. Presented by DR. TOULMIN GAINES, Mobile, Ala.

M. T., a white girl, aged 10 years, had a denuded area on the left lower eyelid which involved one-half of the eyelid.

DISCUSSION

DR. WILLIAM H. MOOK, St. Louis: This case began as alopecia; later a small red line appeared at the border where the lesions had fallen out. When we saw the case today, there was only a single, slightly triangular lesion. The hair follicles seemed to be entirely destroyed. There was no pus or follicular involvement. It is difficult for me to make a diagnosis on one examination, but the case impressed me as looking like a very superficial epithelioma. If the patient were an older person, I think this is the diagnosis I should make. The condition looked more like a growth to me than an inflammatory lesion, and I should consider it a very superficial or even a benign cystic epithelioma.

DR. TOULMIN GAINES, Mobile, Ala.: When I first saw this patient there was just the alopecia, with one fine line like a little, telangiectatic line. I used a Kromayer lamp, well protected with thick black paper, and produced an erythema

which disappeared and left the line looking just the same. Later the line seemed to become broader; thinking the condition was dermatitis, I used a mild salicylic acid and sulphur ointment, which apparently benefited the patient as long as I used it. The mother was disturbed because the hair fell out, and I prescribed pilocarpine. The mother said that when she used the ointment the inflammation disappeared but recurred when she discontinued its use. I have felt that the condition might be a small area of lupus erythematosus, and several doctors here suggested this. I should like to hear further discussion on this possibility.

DR. JACK JONES, Atlanta, Ga.: It seemed to me just a case of pulling the hairs out.

DR. HOWARD HAILEY, Atlanta, Ga.: The portion of the lid which is devoid of hair is definitely enlarged. I, too, do not think the lesion an inflammatory one and wish to suggest that it is lymphangioma. Pressure of the nevus has produced trophic changes, with resultant alopecia. Exercising proper precautions, I should destroy the lesion with radium.

BLASTOMYCOSIS. Presented by DR. H. E. MENAGE, New Orleans.

P. D., a white man, aged 56, was treated for a small, pustular, crusted, granulomatous lesion on the left ala in April, 1929, with unfiltered roentgen rays. The lesion almost healed, but the patient neglected treatment for one year and returned to the clinic with typical blastomycosis involving the eyelids, eyebrows, nose and cheeks.

He is now receiving roentgen therapy for erythema.

DISCUSSION

DR. OLIVER S. ORMSBY, Chicago: Clinically the case is blastomycosis. Tuberculosis verrucosa cutis could be considered, but I have never seen it spread so extensively in so short a time. The tuberculous lesions are less exudative, and usually there is little inflammatory reaction. There are occasional miliary pustules in the margin and elsewhere. In this case there are miliary abscesses in the margin of the lesions. These abscesses are more purulent than is usual in blastomycosis. I have seen cases in which it was extremely difficult to demonstrate the Blastomyces for some time, and I have seen cases that resembled epithelioma. Histologically, epithelial hyperplasia is the most striking feature in blastomycosis.

Syphilis can hardly be considered. Even though the organisms have not been found, I think we should consider the case one of blastomycosis.

DERMATITIS EXFOLIATIVA. Presented by DR. RALPH HOPKINS, New Orleans.

L. B., a white man, aged 55, was treated for mitral decompensation six months before presentation. He showed a generalized, exfoliative eruption of three months' duration.

Following an automobile accident, three months later, he was admitted to the medical ward of the Charity Hospital for mitral decompensation. His blood pressure was 100 systolic and 60 diastolic. Edema of the lower extremities, accompanied by itching, was noted. The patient returned to the hospital, to the department for cutaneous diseases, with generalized edema, inflammatory eruptions over the body and extremities and enlarged nodes in the inguinal region. He died on Dec. 2, 1931. The temperature ranged from 97 to 94 F.; the blood pressure, from 100 systolic and 60 diastolic to 80 systolic and 60 diastolic. The phenolsulphonphthalein test showed 65 per cent. The blood count revealed: red cells, 4,000,000; hemoglobin, 60 per cent; white cells, 7,500; small mononuclears, 28 per cent; large mononuclears, 9 per cent; eosinophils, 4 per cent; neutrophils, 59 per cent. The Wassermann reaction was negative; nonprotein nitrogen was 35: the urea, 15.2; the creatinine was 1.32, and the sugar, 100.

A specimen taken for biopsy from an inguinal node revealed acute hyperplastic adenitis. The gross necropsy showed multiple submucosal gastric hemorrhages, pulmonary edema and acute gastric ulcers.

Microscopic examination of the liver showed marked changes, with hardly a liver cell in a field. There was also fatty degeneration of the liver, as from a toxic drug.

DISCUSSION

DR. HOWARD MORROW, San Francisco: I was much interested in this man, who presented an exfoliative dermatitis which simulated dermatitis following treatment with arsphenamine, but the amount of lymphatic involvement was much greater than one sees in postarsphenamine dermatitis. Furthermore, there is no history of therapy with this drug. I think the case should be classed as one of lymphoblastoma; until we have sections of the glands and of the skin we shall be unable to make a more definite diagnosis. A diagnosis of lymphoblastoma would cover Hodgkin's disease and various types of changes in the blood. Instances of these conditions are comparatively rare, but we recognize more of them now than we did a few years ago, because we study them more carefully. Years ago they were classed with exfoliative dermatitis. I think the prognosis is bad.

DR. OLIVER S. ORMSBY, Chicago: I wish to call your attention to some other patients with somewhat similar disorders. There is no doubt that a large number of erythrodermias that we have not been able to classify belong in the group Dr. Morrow has mentioned. It sometimes takes several years for adenopathy and blood changes to occur which enable us to diagnose a case properly. For example, two or three years ago we showed, before the Chicago Dermatological Society, two patients with what clinically appeared to be Hebra's pityriasis rubra. There was a generalized, fine, scaling eruption; the skin had undergone a yellowish-brown discoloration, and closing the eyes was difficult on account of the tightness of the skin. One of the patients had about 75 per cent small lymphocytes and a leukemic blood picture. The blood count of the other showed evidence of the condition but had clinical symptoms of the same character. About three years after presentation I saw the second case at Dr. Wile's clinic in Ann Arbor, and at that time a leukemic blood picture had also developed. Both of these cases clinically were classic examples of Hebra's pityriasis rubra. Another patient whom I saw about three years ago had a general erythrodermia with little scaling but distinct redness. There was a moderate amount of adenopathy but no change in blood picture, and we classified his condition tentatively in the group of lymphoblastomas.

Similar conclusions were arrived at after an examination at the Mayo Clinic. Within the last four weeks leukemic blood changes have developed, together with general glandular invasion. The new developments followed exposure to sun and wind on an exhausting automobile trip.

These cases, with many others, seem to prove that a large proportion of the cases of exfoliative dermatitis which in the past have been difficult to diagnose will eventually fall in the group of lymphoblastomas discussed by Dr. Morrow.

DR. PAUL A. O'LEARY, Rochester, Minn.: A valuable method of diagnosis in this type of disease lies in the process of development which will permit us occasionally to diagnose these cases before we can do so by histologic examination of the glands or of the skin. I refer to a detailed examination of the blood cells. Hematologists are able to diagnose certain cases of Hodgkin's disease and the leukemias by study of the character of the predominating blood cells. I have had the opportunity to check up on several patients with lymphoblastoma in whom the hematologists made a diagnosis of Hodgkin's disease which we could not confirm by biopsy. Subsequent observations confirmed their findings. Like Dr. Ormsby, I believe a diagnosis of lymphoblastoma is warranted in this case.

DR. RICHARD S. WEISS, St. Louis: I want to ask Dr. Ormsby what his present position is on the question Dr. Engman, Sr., brought up when we first

began to recognize lymphoblastoma. Does chronic inflammation of the entire skin lasting for several years produce the changes in the blood characteristic of leukemia, and does the skin develop lymphoblastomatous changes, or is the leukemia primary? It appears to me that chronic inflammation of the entire skin persisting over a long period of time, months and sometimes years, may produce leukemia. Perhaps Dr. Ormsby will tell us what his position on this phase of the subject is at present.

DR. OLIVER S. ORMSBY, Chicago: We have had this question in mind for a long time, but I do not think it can be answered at present. It is possible that a long continued inflammation of the skin could produce this blood picture, just as the blood picture can produce changes in the skin. I have recorded two patients who had parapsoriasis and leukemic blood changes and believe it is difficult to determine the relationship, if any.

DR. CHARLES C. DENNIE, Kansas City, Mo.: In arsenical dermatitis, during the height of the eruption careful study of the blood picture will often reveal from 4 to 6 per cent myelocytes in the blood. After the patient has recovered from the dermatitis, these cells disappear from the blood stream. This is an indication that the inflammation in the skin might cause the blood changes. In all of these cases the percentage of eosinophils was from 5 to 30 per cent.

DR. RALPH HOPKINS, New Orleans: A surprisingly high percentage of eosinophils has been found in these cases in New Orleans. I am afraid to mention the percentage for fear you may think I am drawing on my imagination, but one of our cases for a short time showed 40 per cent of eosinophils.

DERMATITIS AND LYMPH STASIS. Presented by DR. JOHN A. DEVRON, New Orleans.

L. A., a white woman, aged 45, had been treated during the week before presentation for lymph stasis and dermatitis produced by rubbing her feet against her ankles.

She has a circumscribed lesion on the dorsum of each ankle.

DISCUSSION

DR. OLIVER S. ORMSBY, Chicago: I think we all see many cases similar to this, and the condition is of much interest. The patient had symmetrical lesions on the elbows and knees and similar lesions on the dorsal surfaces of the fingers, on the hands and about the ankles. There are two disorders to consider, symmetrical keratoderma or neurodermatitis. The latter now includes numerous forms of dermatitis outside the limits outlined by Brocq and probably includes cases belonging elsewhere. Multiple patches of keratoderma occurring on the hands, elbows and knees are not infrequently seen and resemble this case but are less inflammatory and are devoid of subjective symptoms. The type under discussion is not that described by Michael, in which the lesions are small and limited to the hands. On account of the evident inflammatory reaction together with itching, the case under consideration would probably be classed as neurodermatitis.

DR. HARRY M. ROBINSON, Baltimore: After all, the name neurodermatitis does not give us much of an inkling as to its etiology. In a few of my cases a smear examination has shown mycelia. I think these cases are of the eczema type. I would like to ask Dr. Ormsby why he considered the possibility of keratoderma. The condition is slightly inflammatory and scaly, and that should rule out keratoderma.

DR. ISAAC R. PELS, Baltimore: While substantiating Dr. Ormsby's diagnosis, I wish to refer to a few points that have been valuable to me in making the diagnosis of neurodermatitis. I have found it valuable to ask patients with neurodermatitis whether they had preliminary itching and whether the eruption followed the itching, the eruption being due to traumatization on the part of the patient. Another point that assists in the diagnosis, in my experience, is that most patches

are well defined. For a working basis and in order not to quibble over terms, I prefer to call the well defined patches without secondary lesions neurodermatitis and those with ill defined patches and with secondary changes neurodermatitis, because of the presence of trauma.

DR. OLIVER S. ORMSBY, Chicago: I think it is valuable to differentiate neurodermatitis from eczema and other forms of dermatitis, as its management is different. As Dr. Pels stated, neurodermatitis is always preceded by itching, and the trauma of scratching develops the lesions. As I previously stated, I believe the present tendency is to include too many conditions under the heading of neurodermatitis, and the same is true of allergy. The internal administration of arsenic, together with properly selected topical agents, is of value. Roentgen therapy is also of value but must be used with caution.

DR. JEFFREY C. MICHAEL, Houston, Texas: The lesions in this case had an inflammatory feature which was not present in the condition that I described. Dr. Ormsby, who saw one of my cases, will agree, I am sure, that there was no resemblance between the lesions in this case and those in my case.

ALOPECIA (UNIVERSAL). Presented by DR. J. N. ROUSSEL, New Orleans.

H. M., a white boy, aged 10 years, had a universal alopecia. There had been four recurrences of this disorder during the four years before presentation.

DISCUSSION

DR. J. N. ROUSSEL, New Orleans: I saw the patient about a year ago. His hair has fallen out three times. Recently it started to grow again, but I think it is now falling out once more. He had a fairly good growth a short time ago, but it has practically disappeared. We tried to have a basal metabolic rate taken, but did not learn much from it. The Wassermann reaction of the blood was negative, as was every other test. We tried various remedies; he seemed to get better, but then he had a recurrence. We used barium sulphite, 1:5,000, locally.

DR. EVERETT S. LAIN, Oklahoma City: I should like to get the reaction of some of our more experienced American dermatologists regarding the etiology of alopecia areata. Last year I learned that some of the English dermatologists, particularly Dr. Barbour, are of the opinion that many of these cases are due to focal infection. I cannot endorse that opinion, but in this case the mother said the child's adenoids had been removed; he still has bad tonsils. The patient clearly breathes through his mouth, and the question of removal of his tonsils might well be investigated.

DR. C. B. ERICKSON, Shreveport, La.: A great deal of work on alopecia areata was done at the New York Skin and Cancer Hospital by Dr. Throne and his associates. At Copenhagen I think they reported that about 75 per cent of a series of 300 patients with alopecia areata had a retention of metals, namely, arsenic and lead, which they demonstrated in appreciable quantities in the urine. I have never been able to find out where this metal comes from. I should like to inquire whether any one present has had experience along this line.

DR. DUDLEY C. SMITH, University, Va.: I have seen one case of universal alopecia areata following bilateral orchitis complicating mumps. I am not sure, though, whether or not there was any relationship.

DR. RICHARD S. WEISS, St. Louis: I presume most of the discussers have been referring to alopecia areata as it occurs in clinical practice. Some one referred to cases in which there was supposed to be retention of a heavy metal and in which the patients recovered after the use of sodium thiosulphate. I have seen many patients in Dr. Engman's clinics who recovered after any treatment that was given and a small number who did not show any result no matter what was used. I think that alopecia areata has a tendency to disappear no matter what is done.

SYPHILIS: ANNULAR LESION ON THE FOREHEAD. Presented by DR. T. A. MAXWELL, New Orleans.

J. M., a white woman, aged 50, presented an annular, serpiginous lesion on the forehead. The Wassermann reaction was strongly positive.

DISCUSSION

DR. HARRY M. ROBINSON, Baltimore: The lesion appeared to be one of nodular syphilis of the serpiginous type, such as we see in late forms of the disease. I know little about leprosy, but the lesions in such cases as I have seen do not conform to this type of lesion. The blood Wassermann report was unknown to me when I diagnosed the lesion syphilis.

DR. HOWARD MORROW, San Francisco: I looked on the case as one of annular syphilid. I thought of the possibility of lepra, but to me the condition was so clinically typical of syphilis, with the 4+ Wassermann reaction, that I decided it was an annular syphilid. If there are changes in sensation, it will be a little more interesting.

DR. JEFFREY C. MICHAEL, Houston, Texas: Sensation was normal in the lesion.

DR. J. N. ROUSSEL, New Orleans: I should like to know if it is not a fact that in anesthetic cases of leprosy we find a positive Wassermann reaction in at least 75 per cent. I have seen a good many cases, and they have all shown a positive Wassermann reaction.

DR. HOWARD MORROW, San Francisco: Yesterday Dr. Mook and I spent the day with Dr. Denny at Carville and the subject of leprosy was discussed. We have found on the West coast that about 80 per cent of the cases of macular lepra show a positive Wassermann reaction. Cases of nerve leprosy give a positive Wassermann reaction in only about 15 to 18 per cent, and it was interesting to see and have Dr. Denny verify this percentage. He was of the opinion that the positive Wassermann reaction in nerve leprosy was always under 30 per cent.

DR. JEFFREY C. MICHAEL, Houston, Texas: I believe that Kolmer has published an article on the subject, and, as I remember, his conclusion was that a patient with leprosy gives a positive Wassermann reaction only when he has syphilis in addition to leprosy.

DR. J. N. ROUSSEL, New Orleans: I should like to have this point settled. Is it your opinion, Dr. Morrow, that anesthesia is a sine qua non in these cases?

DR. HOWARD MORROW, San Francisco: Patients with this type of lepra may be hyperesthetic for months without any changes whatever, but anesthesia develops finally. I feel certain that there are always changes in macular lepra after months and years, but the condition may be present for many months without showing any changes.

DR. RALPH HOPKINS, New Orleans: The anesthesia in leprosy is not always perfect. More often it is just an insensibility to pain, with an abolishment of the epicritical sensation but not of the protopathic sensation, and the anesthesia may be regarded as a constant symptom of the circinate lesions found in anesthetic or nerve leprosy, but it cannot be regarded as a constant symptom of the macular lesions that are found in the nodular type of leprosy, when the patches of the eruption are not circinate but are solid. I do not think the diagnosis of leprosy should be excluded in the nodular cases because of the absence of anesthesia or the presence of pain. The macular lesions are not nearly so likely to be anesthetic as are the annular patches that accompany the nerve type of leprosy.

SCLERODERMA. Presented by DR. J. N. ROUSSEL, New Orleans.

B. J., a Negress, aged 18, presented a pigmented scleroderma of the legs and arms. There had been improvement under thyroid therapy.

SCLERODERMA: LEUKODERMA. Presented by DR. M. T. VANSTUDDIFORD, New Orleans.

B. Z., a Negress, aged 40, presented typical scleroderma of the arms and neck associated with leukodermic areas, which were most prominent on the neck, shoulders and chest. The basal metabolism on Jan. 17, 1931, was —20. Under thyroid therapy the lesions had become less sclerotic, and on Oct. 27, 1931, the basal metabolic rate was + 5.

DISCUSSION ON PAPERS OF DRS. ROUSSEL AND VAN STUDDIFORD

DR. WILLIAM H. MOOK, St. Louis: The interesting thing in these two patients is that in one there is a hyperpigmentation with the scleroderma and in the other destruction of pigment, which frequently happens in Negroes. We have seen a number of similar cases in St. Louis.

DR. PAUL A. O'LEARY, Rochester, Minn.: I was asked about the feasibility of doing a sympathectomy on the first of these two patients, the girl with the Raynaud syndrome with a moderate degree of sclerodactylia and scleroderma. When we reported our results on the surgical treatment of scleroderma, we referred to the group of patients who had Raynaud's syndrome preceding the scleroderma and sclerodactylia. The girl has a definite Raynaud's syndrome, but it developed after the scleroderma. The case is, therefore, not suitable for sympathectomy. We see two and perhaps three types of scleroderma. In the group with the preceding vascular disturbances in which sympathectomy is indicated and carried out, the improvement in the scleroderma is rapid. The operation in cases with secondary or slight vascular complications has not been successful.

DR. W. E. EASTLAND, Oklahoma City: For the diffuse type of scleroderma treated in the Lain-Roland Clinic in past years, we have used radium water intravenously. Two cases in particular showed most favorable results. The trunk from the ensiform process up, including the neck and arms, had a diffuse, rather marked induration. There was a definite limitation of motion in the elbow joints, making it impossible to extend the arms entirely. There was also considerable limitation of the movements of the neck and head. The respiratory movements were slightly impaired.

The treatment was in the form of radium water given intravenously, in doses of from 10 to 25 micrograms. This preparation was made by the United States Chemical Company of New York. In both cases, the limitation of movement of the neck and arms was improved at least 50 per cent, and respiration was much easier. The tissues lost their boardlike consistency.

Since radium, when taken internally, as by the patients who pointed brushes on their tongues in preparing the faces of watches and clocks, has caused bone necrosis and death, I do not advocate its use.

DR. EVERETT S. LAIN, Oklahoma City: In reference to the radium water which we used in the cases of scleroderma mentioned by Dr. Eastland, before using the radium water we tested it on photographic plates. It proved to be strongly radio active, sufficient to make an imprint on the photographic plates.

DR. J. N. ROUSSEL, New Orleans: I wish to ask particularly about the case of the young Negress who has marked myositis. When she was first seen here, the entire musculature was as hard as wood. We thought at one time that the condition was myositis ossificans. I wish to know if this condition is common in scleroderma.

DR. HOWARD MORROW, San Francisco: I think that cases of scleroderma are occasionally associated with scleromyositis and that frequently the toxin, or whatever it is, of the infection stops in the muscle and spreads from the muscle to the skin. Sometimes the involvement of the musculature is secondary to the cutaneous involvement, and occasionally we find the two together. Whatever poison causes the change in the muscle causes the change in the skin, and the condition is dermatomyositis.

KERATOSIS FOLLICULARIS (DARIER'S DISEASE). Presented by DR. M. T. VAN STUDDIFORD, New Orleans.

S. J., a Negro, aged 32, a native of Louisiana, was admitted to United States Marine Hospital No. 14, on Feb. 8, 1930, the chief complaint being sores on the buttocks. There was a history of gonorrhea at 17 and at 32 and of syphilis at 28, for which he had received treatment.

At the age of 13 he noticed a roughened appearance of the skin over his chest and face. Eight years later (1917), small granulomatous masses with a tendency to ulcerate and bleed appeared on each buttock. These were not disabling enough to keep him from being drafted into the army. While in the army he was given five doses of arsphenamine, which seemed to exert a favorable influence on the ulcerations but did not heal them. Cauterization of the masses two years before presentation gave only temporary relief.

For the past two years the masses had increased until walking was uncomfortable.

On examination the patient presented a normal physical condition with the exception of the cutaneous lesions, keratosic plugs which were situated over the forehead, face, chest, back and arms, involving over half of the surface of the skin. On the buttocks were healing, scarred areas, the result of cauterizing doses of radium. On the extensor surface of both legs were horny growths, varying in size from 1 to 3 cm. in diameter. The hard palate was covered with a peculiar lacelike design, dotted with enlarged follicles.

Pathologic sections confirmed the diagnosis of Darier's disease.

DISCUSSION

DR. WILLIAM H. MOOK, St. Louis: The condition was an excellent example of Darier's disease; an especially interesting feature was the condition of the hard palate. There were small, annular, fretwork lesions that were absolutely characteristic of lichen planus. If there had not been the cutaneous lesions, I think we should have diagnosed the condition as lichen planus of the mouth. There were some papules, but the fretwork of small lesions was absolutely typical of lichen planus. We have had several cases of Darier's disease in St. Louis in white people. This is the first case I have seen in a Negro. All the patients had similar funnel-shaped lesions, but the lesions over the body were typical of Darier's disease.

DR. ISAAC R. PELS, Baltimore: I have at the Scientific Exhibit photographs of a fairly early instance of Darier's disease in a girl; I wish we had them here to compare with this case. This patient was interesting to me from the standpoint that he apparently had severe acne many years ago, and he still has some evidences of it on his back. This apparently has made the lesions in the center of the back slightly different from what we should expect. We see there some epidermal plugs with the papules. Naturally one tries to find what the basis of this kind of condition is; when I looked up the literature in connection with our patient, whom I saw two or three years ago, I found that an Italian observer had made some pharmacodynamic tests. On the basis of his observations Dr. Paul Clough made the same type of tests on our patient, but his results were not particularly gratifying so far as the endocrine system was concerned. Nevertheless, because the endocrine apparatus had possibly been associated in producing the changes, I thought it might be of interest to mention this fact.

DR. WILLIAM H. MOOK, St. Louis: Darier's disease is primarily a keratosis of the follicles. The lesions in the mouth in this case are all vesicular, even on the hard palate, but this man showed, in addition to Darier's lesions, lesions that simulate lichen planus. The lichen planus-like lesions were superimposed on the others. The lesions on the groin, buttocks and the perineum, plus the follicles and keratosis over his body, were absolutely typical of keratosis follicularis. There is no doubt that the cutaneous lesions are typical of Darier's disease, but I wish to call attention to the peculiarity of the lesions in the mouth. They may be due to irritation from smoking or some superimposed infection.

Dr. Isaac R. Pels, Baltimore: Has Dr. Mook found lesions in the mouth in all of his patients? We found none in the patient of whom we have photographs.

Dr. William H. Mook, St. Louis: I think not in the early stages, but the oral lesions develop as the disease advances. This has been true of practically all of our cases.

Dr. Howard Hailey, Atlanta, Ga.: Eight years ago I reported three cases of Darier's disease. None of the patients had lesions in the mouth. Two of them were from the same family, a brother and a sister. The brother resided in another city; the local doctor in a recent report said there had been no recurrence of the lesions of Darier's disease since roentgen therapy. I went to see the patient and found a young man with a skin exhibiting marked roentgen sequelae. The third patient was a Negress who had undergone a double amputation for severe pain in her feet. I believe Darier's disease is a nevus.

Dr. M. T. Van Studdiford, New Orleans: In one of the first cases reported by Omerod and MacLeod, in 1904, there were lesions in the mouth. The case presented today was almost identical with that case.

Dermatitis (Vesicular). Presented by Dr. H. E. Menage, New Orleans.

O. N., a white man, aged 43, presented an acute, erythematous, vesicular eruption on the dorsa of the feet and hands. He had been treated for recurrent attacks in various clinics of the Mississippi Valley.

DISCUSSION

Dr. Howard Morrow, San Francisco: Dr. Ormsby and I had a discussion about this patient; I think I am courageous to start the ball rolling ahead of him. There are cases that we see frequently, but we are unable to make positive diagnoses. In the group would be included various types of eczema, epidermophytosis and trichophytosis. I should like to discuss this case from the standpoint of treatment. I do not know why, but these cases are nearly all associated with an epidermophytosis, particularly the sodden type in the webs of the small toes, and, until we get rid of that this type of eczema or dermatitis, will continue to recur. I have found that patients got worse after the use of almost every type of ointment. I have developed a routine of painting these areas with crude coal tar and reapplying it at least twice a week. If there is much dermatitis after the coal tar wears away, I apply a dressing saturated in calamine lotion; this I change every twenty-four hours, and about twice a week I apply the crude coal tar. From my experience I discover that patients make better progress under this treatment than when any type of ointment is used.

For the tinea-like condition between the webs I have stopped using ointments and for a number of years have been applying some dye preparation. I use a dye containing 1 per cent gentian violet and 1 per cent brilliant green in a 50 per cent solution of alcohol; this is used the country over under various names. It is applied on a swab about once a day, and in the majority of cases the tinea in the web will clear up within a month or two.

Dr. Oliver S. Ormsby, Chicago: I am in perfect accord with all that Dr. Morrow has stated.

In a case such as this, with Epidermophyton or Trichophyton infection between the toes, it is not at all unlikely that the dermatitis occurring elsewhere is connected with this infection. This type of dermatitis, however, I do not believe should be classed as epidermophytid or trichophytid. The trichophytids, for example, have an acute course, clear up within from ten days to three weeks and do not recur. The common cause of the infection is kerion of the scalp. When the lesions becomes markedly inflamed, Megalosporon ectothrix leaves the scalp, gets into the blood and locates in the skin. On account of the hypersensitiveness of the skin, Megalosporon ectothrix remains in it a short time and then disappears. It has been experimentally proved that the micro-organism is in the blood

twenty-four hours before the eruption occurs, and that it remains in the skin for about the same length of time. The eruption produces lesions that look like seborrheic dermatitis or psoriasis, as a rule. Occasionally an eruption simulating lichen spinulosus occurs. Any of these, except the last, clear up within from ten days to three weeks. The horny spine type may last several weeks.

I think we should reserve the term "trichophytid" for these types of eruptions.

Concerning treatment, we have found that when grease is not tolerated well, a crude coal tar preparation with collodion and acetone, as used by our Minneapolis colleagues, is effective. The mixture is painted on and remains like a varnish; it is agreeable to employ.

DR. RICHARD S. WEISS, St. Louis: Dr. Ormsby said the eruption was not epidermophytid or trichophytid, and I wish to add that I do not think it is an allergic dermatitis.

DR. J. N. ROUSSEL, New Orleans: I have always classified this disorder as patch eczema, for want of a better name, but I wish to say that I do not believe that the trichophytids have anything to do with it. I think that finding an egg in the grass and concluding that there is a hen's nest there is going too far. The only patients I have ever known to get well and stay well are those whom I have treated internally. Hypodermic injections of cacodylate of soda, 5 to 7.5 gr. (0.325 to 0.488 Gm.) every three days, will cure them, and they will remain well after five or six doses. As a rule 5 gr. (0.325 Gm.) is sufficient.

DR. C. F. LEHMAN, San Antonio, Texas: Could this be a vesicular manifestation of a neurodermite? When these lesions recur, they are so commonly in the same place; I wonder if they have not a neuropathic origin. I have used sodium sulphate in these cases. I think not all of them can be explained on a neurotrophic basis, but I believe that some of them can. I have had some local reaction from injection of trichophytid. I think some cases are allergic, but I believe that many are neurogenic, precipitated by internal conditions.

DR. BEDFORD SHELMIRE, Dallas, Texas: Since there is a possibility that the dermatitis in this patient is caused by some exogenous substance with which he comes in contact, I suggest that one hand and forearm be covered with a zinc paste bandage for two weeks. If the bandaged area heals in this interval, it can be assumed that the dermatitis is of external origin. Such a procedure does not determine the offending cutaneous irritant. If healing results, that suggests that the eruption is caused from contact with some eczematogenous substance and stimulates search for this excitant.

The varnish spoken of consists of crude coal tar, collodion and acetone in equal amounts. The preparation is painted on with a brush or swab and forms a varnish-like coating.

A CASE FOR DIAGNOSIS (LUPUS ERYTHEMATOSUS?). Presented by DR. M. T. VAN STUDDIFORD, New Orleans.

D. A., a Negro, aged 33, stated that about three years ago, while he was working in a factory in which second hand burlap bags were made, there developed on the back of each hand a deep redness which was tender and dry and itched slightly. He soon became extremely weak, with stinging and pricking sensations of the skin over the entire body. His skin became very sore; within three months there was a generalized dermatitis somewhat similar to that which first began on the back of his hands. At first it was dark red; then it became exceedingly dry and scaly. The skin was "hard."

The bags which he was handling had been used and had contained flour, sugar, coffee, grain, etc. His duty consisted of cleansing them in preparation for refilling. None of the other men handling the bags had similar cutaneous lesions.

The condition had been present and gradually growing worse for three years.

The Wassermann reaction was negative. Medication had been chiefly internal and had been administered by various doctors.

The patient at the time of presentation had a generalized eruption over the lower extremities, with some pink papules, and on the hard palate there were lesions resembling lichen planus. The pink telangiectasis and tissue paper appearance of the skin was generalized.

DISCUSSION

Dr. Paul O'Leary, Rochester, Minn.: I believe this is the most startling case presented today. In the differential diagnosis I considered disseminate lupus erythematosus first; second, poikiloderma vasculare atrophicans; third, the similarity between this patient and the patient Dr. Engman presented last year at the meeting of this society in St. Louis. I do not recall the name of the patient. I think the predominance of evidence is in favor of disseminate lupus erythematosus, but before making that diagnosis I should wait until a complete examination has eliminated the possibility of one of the lymphoblastomas. The alopecia, the marked loss of weight and the marked asthenia all fit in well with the diagnosis of disseminate lupus erythematosus.

Dr. A. L. Glaze, Birmingham, Ala.: A case of dermatomyositis which I observed showed at one stage an eruption markedly resembling that noted today in this case, save that in large measure it was confined symmetrically to the neck, shoulders and upper extremities. Study of the case under consideration from that point of view might be enlightening. If marked muscular weakness is present, the taking of a specimen of the muscle tissue for biopsy would seem to be indicated.

Dr. Oliver S. Ormsby, Chicago: The first cases of poikiloderma that were described in this country were recorded by Dr. John E. Lane, and he included a patient whom I saw. A characteristic symptom is the occurrence of patches resembling a healed radiodermatitis. However, that type of lesion is not always present. Some cases have been reported that have been considered generalized lupus erythematosus, others lichen planus, and so on, but all have atrophy, hyperpigmentation and telangiectasia. This patient does not present the typical symptoms of poikiloderma. I have seen three patients with atrophy, hyperpigmentation and telangiectasia; I studied one patient carefully, histologically and otherwise, without being able to diagnose the condition. One of the patients has been seen by eminent men here and abroad, with the same result. It may be that this case belongs to the as yet unclassified group.

Dr. William H. Mook, St. Louis: I wish to confirm all Dr. Ormsby said and to mention one point a little more in favor of lupus erythematosus. That is, the lesions on the thighs, and more especially those on the lower part of the legs, are follicular, scaling patches, almost keratotic in the follicles, which I consider a little more in favor of a diagnosis of lupus erythematosus. On the other hand, I think no diagnosis can be made until the case is studied further. The man has lesions on his hard palate that resemble those of lupus erythematosus.

Pellagra. Presented by Dr. H. Turner, New Orleans.

S. W., a Negress, aged 27, stated that on about the first of March, 1931, dermatitis developed on the back of the hands and on the anterior part of the legs, with symptoms of diarrhea, weakness, stomatitis and vertigo. She was admitted to the hospital at that time with the following laboratory observations: red blood cells, 2,500,000; the white cells, 3,500; urine, normal, and the Wassermann reaction, strongly positive. Gastric analysis showed: free hydrochloric acid, 13; total hydrochloric acid, 40. The diet for pellagrins was ordered. Dilute hydrochloric acid and a solution of potassium arsenite (Fowler's solution) were administered by mouth; six intravenous doses of neoarsphenamine were given and also a mixed treatment with mercury and iodides.

The patient was discharged in good condition at the end of two months. She had gained weight, the dermatitis had disappeared, the symptoms were relieved, and the blood count was raised to 3,085,000 red blood cells.

She was readmitted on Oct. 11, 1931, with these symptoms: dermatitis of the hands and legs, loss of weight, diarrhea, weakness and stomatitis. The Wassermann reaction was negative. The blood count was 1,850,000. Gastric analysis showed the free hydrochloric acid to be 15; the total hydrochloric acid, 60. The urine was normal; chemical examination of the blood showed: nonprotein nitrogen, 22.2 mg.; urea nitrogen, 10.5 mg.; creatinine, 1.2 mg.; uric acid, 4, and sugar, 80 mg. She was given the diet for a pellagrin, a solution of potassium arsenite, dilute hydrochloric acid and pills of ferrous carbonate, U. S. P.

PELLAGRA. Presented by DR. H. TURNER, New Orelans.

J. R., a Negress, aged 36, stated that her disorder began about June, 1931, with loss of appetite, loss of weight and dermatitis.

The laboratory observations were as follows: The Wassermann reaction was negative; the blood pressure was 210 systolic and 130 diastolic; phenolsulphonphthalein was 50 per cent. Chemical examination of the blood showed: nonprotein nitrogen, 26.6 mg.; urea nitrogen, 12.7 mg.; creatinine, 1.2 mg.; sugar, 95 mg. Gastric analysis showed: free hydrochloric acid, 40; total hydrochloric acid, 68. The urine was normal. Medication consisted of cod liver oil, elixir of quinine, iron and strychnine and liver extract, and her diet was restricted to that of patients with pellagra.

PELLAGRA. Presented by DR. H. TURNER, New Orelans.

E. B., a Negress, aged 32, stated that her trouble began about Oct. 1, 1931, with a general weakness, stomatitis, loss of weight and dermatitis of the hands and legs.

The laboratory observations were as follows: The Wassermann reaction was negative; the urine, normal; the weight, 78 pounds (35.4 Kg.); the blood pressure, 115 systolic and 80 diastolic; phenolsulphonphthalein, 40 per cent. Gastric analysis revealed free hydrochloric acid, 10; total hydrochloric acid, 45. The blood count was: red cells, 2,950,000; white cells, 5,500. Chemical analysis of the blood showed: nonprotein nitrogen, 22.2 mg.; urea nitrogen, 10.7 mg.; creatinine, 1.2 mg.; sugar, 76 mg.

The medication consisted of the routine treatment for pellagra.

DISCUSSION

DR. JEFFREY C. MICHAEL, Houston, Texas: Kirby-Smith and his collaborators reported excellent results from neoarsphenamine in pellagra. Our experience in Houston shows this drug to be valuable. I should like to know what others here think of this medication.

DR. ISAAC R. PELS, Baltimore: What type of "pellagra diet" was used? In Baltimore we have used a large amount of fresh liver in the diet and termed it a "pellagra diet."

DR. M. T. VAN STUDDIFORD, New Orelans: The diet in the Charity Hospital here is high in proteins and beans. The grain carbohydrates and grits are restricted, and large amounts of orange juice, yeast, cod liver oil, dilute hydrochloric acid and solution of potassium arsenite (Fowler's solution) are given. The first patient in this group had just finished a course of arsphenamine before pellagra developed.

DR. J. N. ROUSSEL, New Orleans: In 1910, I was consulted by a Roman Catholic who, in order to observe Lent, had not eaten anything at all. By the end of Lent he had a typical case of pellagra. I gave him lemon juice, and in about ten days he was practically well. Since then I have never given my patients with pellagra anything but lemon juice, and I have yet to see a patient, provided he had not become bedridden, who failed to get well. We give no medicine unless the patient is badly constipated.

DR. BEDFORD SHELMIRE, Dallas, Texas: The dietary theory does not adequately explain the etiology of pellagra. Besides the dietary deficiency, there is probably also an exciting cause. During the summer and fall of 1926, there was in the vicinity of Dallas a marked increase in the yearly incidence of pellagra. The increase in the incidence of this disease was so marked at that time that Dr. Joseph Goldberger made a personal survey of local conditions, which, compared with the present, were extremely good. Although the living conditions of the potential pellagrin are far worse now, due to the depression, the total number of pellagra cases in the same territory does not begin to assume the proportions observed in 1926. I have no figures to substantiate my claims, yet my belief is that the incidence of pellagra this year is no greater than the normal for the past ten years. Theoretically, if the dietary theory alone explained the etiology of pellagra, we should expect a marked increase in the incidence of the disease this year. This apparently has not occurred; not in Dallas, at least.

DR. D. W. GOLDSTEIN, Fort Smith, Ark.: We have seen a marked increase of pellagra in Arkansas, primarily due to dietary conditions there. There have been over 500 cases reported in one county that I know of. The people in this county are in extremely poór circumstances, due to a recent failure of crops.

DR. E. D. CRUTCHFIELD, San Antonio, Texas: I should like to inquire whether an examination of the gastro-intestinal tract has been made in these cases. I am inclined to believe that pellagra is a deficiency disease and not entirely a dietary condition. I think that in many instances the disorder is due to the way food is assimilated rather than to what is eaten. I think that in many instances people are not getting sufficient vitamins to prevent the disease, and that it is due to deficiency in vitamins. I think that all cases of pellagra are practically of the same type, whether they are due to alcohol or are associated with cancer or some other disease; it is important that patients should be studied from the standpoint of gastro-intestinal disturbances. Few patients with the fulminant type of pellagra ever get well. On the other hand, many patients, such as those that developed pellagra during the famine in Arkansas, will get well.

DR. D. C. SMITH, University, Va.: In connection with Dr. Crutchfield's comment that pellagra may be primarily a disease of the gastro-intestinal tract, we know that a number of patients with severe cases of pellagra are incapable of digesting and metabolizing a balanced menu. With this in mind, a few years ago we started treating most of the patients with severe cases of pellagra by frequently repeated transfusions of blood. It was thought that this would supply them, in readily usable forms, with a small quantity of all of the elements required for proper nutrition. The amount, of course, is not sufficient for total nutrition but possibly enough to counteract the patients' own deficiencies. Whole blood contains all the essential proteins, salts and vitamins necessary to combat the disease.

DR. PAUL F. STOOKEY, Kansas City, Mo.: In the normal years in Kansas City we have a few cases of pellagra. Since July 1, 1931, there have been thirteen cases of pellagra in my service.

DR. OLIVER S. ORMSBY, Chicago: My impression that pellagra is an infectious disorder was gained while I was working on a commission studying the disease, in 1910. The work of the Garrison Commission that studied the disease in the South some years later rather confirmed my impression. Goldberger's work followed; this seemed to prove that pellagra was a nutritional disease. There is no doubt that pellagra can sometimes be produced with improper food. Gastro-intestinal disorders that interfere with nutrition are occasionally accompanied by the disease. The alcoholic form of pellagra is undoubtedly produced in this same way, by interference with proper assimilation of food.

Jobling and Peterson found a fungus in the intestinal tract of pellagrins capable of producing a fluorescent substance in the blood which sensitized the skin to the sun's rays. This was a most important discovery and should be confirmed. Jobling and Peterson also found the diet of their patients to consist largely of

carbohydrates, which furnished a proper soil for the growth of the fungus mentioned before.

Our experience in Illinois proved that the skin of pellagrins is sensitive to light and that, while lesions do occur in nonexposed areas, active lesions can be produced by the sun's rays.

All of my private patients suffering with pellagra have had access to proper food; in fact, they have eaten it. Whether or not they have assimilated it I cannot say. On the other hand, there is no doubt that these patients do well when the amount of carbohydrates consumed is reduced and a properly balanced diet is used. This would not rule out the possibility of infection, as improper diet might render the patient sensitive to an infectious organism of some type.

I think an excellent service would be done if investigators in the South, who have access to patients suffering from this disorder, would prosecute further the work that has been done by Jobling and Peterson.

Dr. J. N. Roussel, New Orleans: Patients with pellagra who have apparently had enough to eat are commonly those who eat out of tin cans. I have seen many of these cases; there is no telling how long the food had been in the cans. Many women who have to do their own work will not cook; they live almost entirely out of tin cans.

Dr. Toulmin Gaines, Mobile, Ala.: I once had to take up the cudgels with Dr. Goldberger himself. I gave him such information as I had; I live in a suburb of Mobile, near a community in which there was a large incidence of pellagra. Along the road that led from that community to the suburb where I live pellagra progressed from house to house until it invaded the neighborhood in which I live. In three instances it occurred among those who were apparently well-to-do. The question is whether pellagra is a deficiency disease or whether the conditions in which the pellagrins live produce a susceptibility to the disease. In either case we shall undoubtedly have an increase in the disease due to the prevailing depression.

Dr. Richard S. Weiss, St. Louis: You can put food in front of a person, but that does not mean that he will eat it. We frequently see pellagra in children and young people, and it occurs among what Dr. Engman calls "pickers." One child came from a good family, but he would not eat anything except spaghetti. Usually these youngsters will choose only carbohydrates; the proteins in their diet are extremely limited. These are the subjects who develop pellagra. This has nothing to do with the possible infectious character of the disease, as Dr. Ormsby brought out.

Dr. Tom W. Murrell, Richmond, Va.: Just before he died Dr. Goldberger said he thought there was an unknown factor in this disease and that the best way to handle it was from the dietary standpoint.

Pemphigus? (Herpetiform Dermatitis). Presented by Dr. Ralph Hopkins, New Orleans.

M. W., a "high yellow" Negress, aged 25, had a vesiculosquamous eruption over the face, body and extremities. She was treated for a similar eruption six months before presentation, with disappearance of the lesions. At that time a diagnosis of pemphigus was made, and erythema multiforme was considered.

She had received no treatment during the four months before presenting herself at my office.

DISCUSSION

Dr. Isaac R. Pels, Baltimore: The condition clinically impressed me as being pemphigus, because the vesicles are of the flaccid type, but this fact does not necessarily assure one of the diagnosis. I was able, however, to demonstrate a positive Nikolsky's sign.

With regard to the course of the disease, it was interesting to me to discover that the patient has apparently improved, but I believe it is the experience of nearly

every one that in pemphigus remissions occur. Despite the fact that a diagnosis of pemphigus signifies a lethal outcome, there are some patients who live for a long time. One patient (pemphigus foliaceus) in particular, in Baltimore, has been seen by nearly every doctor along the Atlantic seaboard and has remained practically well for many years. He occasionally has a small vesicle, so that complete disappearance of all lesions has not occurred in his case nor in that of others that I recall who have had partial remissions. One can only speculate concerning the reason these patients improve. I am interested to know what makes these patients with pemphigus improve under medication. Various methods are used in the treatment of the disease; what helps one patient is unsuccessful with others. One important thing reported in Germany has been the irradiation of the gonads, particularly in females. Some of those cases apparently were not pemphigus, because they occurred in extremely young people.

Regarding the phytopharmacologic tests, we are still interested in having these tests go on, for we have a fair amount of proof that they mean, if positive, the diagnosis of pemphigus. The method has not received as yet, however, a thorough trial. Every now and then we receive readings which are incongruous. When the patient dies, for example, the test reads normal How to explain this we do not know, except that we have called attention in our publications to the fact that patients who are about to die sometimes lose all their lesions. There seems to be some curious, protective phenomena taking place in the body. The test itself has not been fully completed, for the pitfalls of the technic are such that it is comparatively a one man test. Sometimes material is added to the blood which brings about false positive reactions. A most interesting fact about some specimens of blood is that these materials come in relatively late and change the color of the blood. The blood may be of the consistency of ink and not the normal, clotted blood one would expect. Whether that is due to chemicals or to long standing or to some inherent qualities of the blood, we do not as yet know. These are questions that Dr. Macht has given attention to and hopes at some time to answer.

In patients who have pernicious anemia the toxic element in the blood responds to irradiation with ultraviolet rays, but this is not the case in the blood of pellagrins. If anything, a specimen on standing becomes more toxic, but we cannot give an explanation of why these differences exist.

BRONX DERMATOLOGICAL SOCIETY

THEODORE ROSENTHAL, M.D., *Secretary*

Regular Meeting, Nov. 19, 1931

HENRY SILVER, M.D., *President*

LYMPHOBLASTOMA (ALEUKEMIC LEUKEMIA). Presented by DR. S. FELDMAN.

A. T., a white man, aged 57, with an irrelevant personal history, about six weeks before presentation, noticed small reddish masses on his chest and back. Four weeks later a sore throat, with difficulty in swallowing, developed and he became gradually weaker. On examination there were bluish nodules, ranging in size from that of a penny to that of a half dollar, that were movable with the skin.

Examination of the blood showed: white blood cells, 2,400; red blood cells, 1,800,000; hemoglobin, 30 per cent; polymorphonuclears, 24 per cent, and lymphocytes, 76 per cent. There were several abnormal forms, including lymphoblasts.

The biopsy revealed round cell infiltration of the middle and lower layers of the corium and subcutis. The cells were uniform in size and shape and were packed closely with very few fibers between. The cells approached closely the type of the large lymphocyte. There were no giant cells or mitotic figures.

DISCUSSION

DR. F. DIASIO: I saw the patient previous to presentation, at the very onset of the disease. The erythematous nodular masses with a few skin-colored lesions inclined me to the belief that the condition belongs to the lymphoblastoma group or to that of mycosis fungoides. A specimen was taken at that stage for biopsy and examined by Dr. Satenstein. His impression was leukemia cutis.

DR. L. CHARGIN: The cellular infiltration in the histologic picture of mycosis fungoides contains many types of cells.

DR. A. ROSTENBERG: I believe that we are dealing here with leukemia cutis. There is no evidence of clinical changes in the skin that warrants a diagnosis of premycosis fungoides.

DR. S. FELDMAN: Although my diagnosis is lymphoblastoma, the histologic study suggests mycosis fungoides because the cells are not uniform.

A CASE FOR DIAGNOSIS (MULTIPLE FIBROMAS?). Presented by DR. S. FELDMAN.

E. S., a woman, aged 61, noticed about three or four years before presentation several painful tumors on the back and on the abdomen. On examination, these tumors were seen projecting partly above the surface of the skin, but were for the most part embedded. They were hard and very tender.

DISCUSSION

DR. C. GREENHOUSE: It is my impression that this case is one of von Recklinghausen's disease rather than of lipomatosis.

DR. A. ROSTENBERG: I cannot make a diagnosis of von Recklinghausen's disease because of the absence of the common epidermal manifestations usually present, such as nevi, café au lait spots and ephelids. I believe the tumors are fibrolipomas.

DR. S. FELDMAN: I believe that Dercum's disease can be ruled out in this case. The lesions are more painful in this case than is usual in simple fibromas. Is it not possible to have a forme fruste of von Recklinghausen's disease with only neurofibromas as well as the forme fruste with nevi but without fibromas?

DR. H. SILVER: By forme fruste of von Recklinghausen's disease is understood the early abortive type of the disease characterized by the total absence of tumors but by pronounced pigmentary changes. In a fully developed case of von Recklinghausen's disease with characteristic tumors, café au lait spots, etc., are never absent. The changes of the central nervous system are observed in both types.

MELANOMA WITH METASTASIS. Presented by DR. G. SPINNER.

R. R., a woman aged 36, had noted for the past several years a blue-black lesion on the outer aspect of the left arm about the size of a dime, which was slightly raised above the level of the skin. About six months before presentation this lesion became irritated and apparently infected. She went to her local physician who incised a very small pustule in the lesion. She went to another physician, who, using surgical diathermy, removed the lesion. Four months later, she began to complain of severe pain in the left arm, extending from the left supraclavicular space down to the finger tips. There was pain in the left axilla and left breast. She also complained of loss of weight.

At presentation, on the outer aspect of the left arm was found a lesion the size of a dime, brownish, atrophic, with a hard fibrous border. Adenitis was present in both supraclavicular spaces and in the left axilla.

DISCUSSION

DR. S. FELDMAN: This patient was found to have tumors in the mediastinum on roentgen examination. The prognosis is grave.

DR. I. LASHINSKY: Biopsy is not to be considered in this case. It is important to determine whether the breast is involved.

DR. A. ROSTENBERG: I believe we are merely speculating about the dangers here. The patient appears to be in good health, and I think that there is nothing about which to be alarmed. I could not feel any tumor masses. The firm, infiltrated scar at the base impresses me as having been left by an innocent nevus removed by electrodesiccation.

DR. F. DIASIO: There are no other evident lesions on the skin such as one would expect if this were a melanoma with metastasis.

DR. C. GREENHOUSE: It is my impression that we are dealing with a treated angioma.

DR. C. LERNER: There is comparatively little danger in removing a gland from the supraclavicular region. In melanomas, metastasis is rapid when the knife is used for biopsy. They should be removed with a cutting current, with a wide and deep excision down to the muscles.

DR. G. SPINNER: This patient has lost considerable weight and has severe pain in the left arm, all dating from the removal of the original lesion, which confirms the impression of a melanoma.

PHENOBARBITAL ERUPTION OF THE MOUTH. Presented by DR. M. HOFFMAN.

A white woman, aged 38, married, stated that a few hours after the ingestion of ½ grain (0.03 Gm.) of phenobarbital, large and small bullae appeared on the mucous membranes of her mouth and lips. These bullae broke down, leaving superficial ulcerations which were extremely painful. No lesions were seen on the body. The patient had experienced a similar attack a few months before presentation following the ingestion of the same drug. The intake of acetylsalicylic acid gave the patient an urticarial eruption.

DISCUSSION

DR. F. DIASIO: I would suggest a therapeutic test with phenobarbital to see if the lesions reappear.

MULTIPLE BENIGN CYSTIC EPITHELIOMA. Presented by DR. HENRY SILVER.

Mrs. R. B., aged 39, born in Turkey, married, the mother of two children, whose personal history did not reveal anything of interest, had an eruption that had begun seven years before presentation on the right thigh with a few tiny papules that were not itchy. At presentation there were lesions situated on the neck, chest, axillae and thighs. The lesions varied in size from that of a pinpoint to that of a millet seed, and were skin-colored or somewhat bluish. They were grouped on the neck. To the palpating finger they were soft. Recently, they had begun to itch. Laboratory tests gave negative results.

Dr. Peck's report on the specimen removed for biopsy follows:

The epidermis was unchanged, except for a slight thickening in places. In the middle layer of the cutis there were a number of scattered cell strands and cystlike structures. The cysts varied in size from that of a cross-section of a sweat duct to ten or fifteen times that size. The cyst wall was made up of from one to two layers of cuboidal or flattened cuboidal epithelium. The cysts contained an amorphous substance that took the eosin stain very lightly. The cell strands consisted of several layers of polygonal epithelium cells with oval or round nuclei. A number of them showed a tendency to form a lumen. The changes in the cutis were secondary to the mechanical pressure of the cysts. Right below the epidermis were chromatophores.

The section was typical of the histologic picture of syringoma.

DISCUSSION

DR. R. BREAKSTONE: This patient has intense itching, which is an unusual finding.

DR. L. CHARGIN: This condition is usually observed in younger persons, although it may be seen in older ones.

A CASE FOR DIAGNOSIS. Presented by DR. M. BERKOVSKY.

J. K., a white boy, aged 5 years, had an eruption which his mother noticed had developed suddenly in July, without any subjective symptoms. The eruption remained practically stationary, and when observed at the Mount Sinai Hospital, presented many circinate and gyrate lesions situated on the trunk, both anteriorly and posteriorly, and also on the thighs. The borders were slightly elevated and were covered with a fine scale. An ointment of 5 per cent ammoniated mercury was applied and produced a severe dermatitis. Following this, bland ointments had been used, and the lesions were involuting. Repeated examinations of the scales for fungi gave negative results.

DISCUSSION

DR. G. SPINNER: It is my impression that this condition is pityriasis rosea.

DR. F. DIASIO: I believe it is either erythema centrifugum annulare Darier or parapsoriasis.

DR. L. CHARGIN: I am unable to offer a positive diagnosis. I am certain, however, that the condition is neither erythema centrifugum annulare Darier nor parapsoriasis. The former begins with a papule and spreads peripherally, clearing in the center. Moreover, it is usually a disease of adults. As to parapsoriasis, these lesions lack that specific type of scaling, the color and the distribution; parapsoriasis is also extremely uncommon in children. My impression is that we are dealing with seborrhea.

DR. F. CROSS: The condition appears to me to be seborrheic dermatitis, and the use of a sulphur ointment would act as a therapeutic test.

PSORIASIS WITH MARKED INVOLVEMENT OF THE NAILS. Presented by DR. ADOLPH ROSTENBERG.

A man aged 39, an Italian, had a vague history of a previous case of psoriasis. Four months before presentation the patient had received antisyphilitic treatment; after six injections of arsphenamine a severe arsphenamine dermatitis developed, for which he was confined for seven weeks in a hospital. At the present time he presented a scaling eruption, located mainly on the lower extremities, consisting of small coinlike lesions and larger scaling patches. The scales were very superficial and were easily brushed off. In addition all of the toe-nails and finger-nails were involved. They were markedly thickened, showing heaped up scaling; they were brittle and showed a dirty grayish discoloration. There was also marked stippling. Examination for fungi gave negative results.

DISCUSSION

DR. L. CHARGIN: I believe that this condition is not psoriasis of the nails but the result of a generalized arsenical intoxication.

DR. T. ROSENTHAL: In view of the stippling, the transverse grooving and yellow-brownish discoloration of the nails, I am inclined to believe that this is psoriasis of the nails. I think that Heller emphasized the discoloration in the diagnosis of psoriasis of the nails.

GENERALIZED ERYTHRODERMIA. Presented by DR. I. M. LASHINSKY.

P. F., a man, aged 27, married, came to our clinic complaining of severe itching all over his body. About one year and a half prior to admission to the clinic, the patient noticed some "pimples" in his armpits, resembling prickly heat. These lesions began to spread and itch. He was treated in several hospitals with sodium

arsenate and sodium thiosulphate and later with roentgen rays, without any relief. On Nov. 7, 1931, he presented generalized erythrodermia with scaliness and a number of small tumor-like infiltrations throughout the entire body.

The laboratory findings were: Wassermann reaction of the blood negative; white cells, 10,900; red cells, 4,940,000; polymorphonuclears, 63 per cent; lymphocytes, 21 per cent; mononuclears, 5 per cent; eosinophils, 8 per cent, and basophils, 3 per cent.

The only topical application that the patient used at presentation was boric acid. He was under our care for about twelve days, and there was considerable improvement.

DISCUSSION

DR. C. GREENHOUSE: In view of the aggravated lesions at the elbows and knees and the lichenification and exaggeration of the skin markings in these areas, I venture the opinion that we are dealing with a generalized neurodermatitis.

DR. C. LERNER: The underlying factor in this case is an allergic condition of the skin that renders the patient sensitive to a multitude of factors in his environment.

DR. I. M. LASHINSKY: It is interesting to note that the patient improved considerably when removed from his surroundings.

NEW YORK DERMATOLOGICAL SOCIETY

E. R. MALONEY, M.D., *Secretary*

Regular Meeting, Nov. 25, 1931

J. F. FRASER, M.D., *President*

A CASE FOR DIAGNOSIS (LICHEN PLANUS). Presented by DR. JOHN E. LANE.

J. A., a man, aged 33, presented a generalized, slightly scaly erythroderma of two months' duration. A few clear pea-sized vesicles had appeared occasionally. The inguinal, axillary and cervical glands were moderately enlarged. The blood count was normal, and the Wassermann reaction was negative. There was some lichenification but no papules typical of lichen planus.

DISCUSSION

DR. E. F. TRAUB: The patient presented definite lichenified papules on the penis, and scattered throughout the entire eruption there seemed to be characteristic lichen-like papules. Owing to the scratching, this condition might be interpreted as lichenification, but some of the papules seemed to be entirely independent of the lines of cleavage of the skin; a distinct violaceous color with the suggestion of milky striation was also present. I should think that lichen planus would have to be ruled out.

DR. W. J. HIGHMAN: The case interests me not so much clinically as etiologically. The elements of the eruption are those of erythroderma, lichen planus, exudative dermatitis and lichenification. Thus the condition may be an essential or a secondary erythroderma, or it may prove to be lichen planus, as various speakers have suggested. The patient has tylosis of the palms. In the Mount Sinai dermatologic service one sees many patients in whom erythroderma is present, irrespective of the nature of the elementary lesions. At present, there are one patient with psoriasis and three others with essential erythroderma. Leaving out the group of cases proved to be due to some form of "lymphoderma," it seems to me that either many patients have erythroderma because of some systemic disease or that some persons tend to have erythroderma as others have eczema, irrespective of the provocation. Is this a racial tendency? At Mount Sinai, the

group of patients in question are of an ethnic type, to which Dr. Lane's patient belongs. In spite of its remoteness, the suggestion is worthy of consideration. The enlarged glands in Dr. Lane's case signify either secondary involvement or causal relationship. If such cases are ultimately proved to belong to the true lymphatic irritations representing a stimulation of the endothelium, they constitute a clinical entity. The course of such cases should be observed, but we may justifiably add to our conception of the erythrodermas the idea that some of them reflect an erythrodermal predisposition in the individual. I hope that this tentative suggestion will be kept in mind by observers who will substantiate or overthrow it.

DR. HOWARD FOX: With no history of local irritation from treatment and without having made serologic or histologic examination, we cannot go far in determining the nature of this condition. An examination of the blood might show leukemia, and lymphoblastomatous changes might be shown in the glands. We have all seen cases like this in which histologic examination showed nothing but simple inflammation. On the other hand, in some of these cases distinct changes in the blood later develop, and clear cases of leukemia result.

DR. C. M. WILLIAMS: Dr. Highman raised the interesting point of the possibility of race influence in the production of this condition. The Jews of New York are not a racial, but a social and religious, group. They come from the most varied regions; some appear to be pure Semites; others are short, round-headed people who seem to show large Alpine and Mongol strains. If statistics of race incidence in disease are to be of value, the word "Jewish" must be discarded in this connection and a more definite adjective employed. The habits and customs of the Jews may predispose them to certain diseases, but this is a social and not a racial factor.

DR. W. J. HIGHMAN: Since Dr. Williams commented on my remarks, I feel free to say what I should not otherwise have mentioned. He is right about the ethnic character of the modern Jew. The majority of the Jews in this country come from Southern Europe and constitute the group most susceptible to this condition. I think that it is a question of Mediterranean background rather than of Semitism, for European Jews are not pure Semites.

LUPUS ERYTHEMATOSUS CONFINED FOR TWENTY YEARS TO THE SCALP. Presented by DR. FRED WISE.

Miss H. M., aged 59, a school teacher, applied for treatment for a condition of the scalp at the Post-Graduate Clinic. She stated that the disease began on the scalp twenty years previously as a small, scaly red spot which gradually increased in size and was accompanied by permanent alopecia.

Examination revealed several circular denuded areas on the vertex and on the occipital portions of the scalp, varying in diameter from ½ inch (1.27 cm.) to 1½ inch (3.7 cm.). These areas were smooth, dusky red, partly glazed, partly covered with dry adherent scales and entirely devoid of hair and of visible hair follicles.

Histologic examination confirmed the clinical diagnosis of lupus erythematosus discoides.

DERMATITIS VENENATA (ORTHOFORM). Presented by DR. R. H. RULISON.

C. H., a pharmacist, aged 45, was presented to show dermatitis venenata and a positive patch test for orthoform. The patient was first seen in May, 1929, at the end of such an attack. Tests made with suspected substances gave negative results. In April, 1930, a similar attack occurred, and again search for the irritant failed. The attack for which the patient was presented began six days previously, and all tests were negative, except the one for orthoform.

The patient gave a history of having had similar attacks at intervals for the past nine years, but during one year in which he did not handle drugs no attacks occurred; furthermore, he had never had an attack while on a vacation. There-

fore, it was thought that the probable cause of the dermatitis was some drug encountered in his work.

Orthoform, or methyl-n-amino-para-oxybenzoate, is almost insoluble in water and is readily soluble in alcohol.

The formula is as follows: $\left\{ C_6H_3 \middle| \begin{matrix} COOOH_3 \\ NH_2 \\ OH \end{matrix} \right.$

DISCUSSION

DR. GEORGE M. MACKEE: This is an interesting finding, and both Dr. Rulison and the patient are to be congratulated on their perseverance. It should be definitely determined, however, whether the condition is one of sensitization or of irritation. That fact can be ascertained by the use of a control and by making tests with high dilutions of the drug. I agree that the eruption is probably due to an idiosyncrasy, but orthoform is said to be an irritant; therefore the eruption either may be due to idiosyncrasy or it may be the result of irritation in the absence of idiosyncrasy.

DR. R. H. RULISON: The case was presented as one in which there was great difficulty in determining the cause, even with the cooperation of an intelligent chemist. Orthoform is known to cause a rather marked reaction in certain persons; sloughing has been known to follow its use. It has been used extensively in powder form for the treatment of throats and in ointment in the dressing of wounds. I think that the patient is probably sensitive to orthoform. Tests with solutions of the drug will be made after the present attack has subsided.

LICHEN PLANUS WITH VESICLES IN A CHILD AGED FIVE YEARS. Presented by DR. FRED WISE.

Florence W., a girl, aged 5, was taken to the Post-Graduate Clinic, in November, 1931, for treatment of an eruption of the hands. She was in good general health. For a period of five months the backs of the hands had presented many inflammatory papules, varying in size from that of a barley corn to that of a lentil, together with several clear vesicular lesions, the latter being about the size of a small French pea. Many of the lesions exhibited the violaceous color, polyhedral outline and distinct umbilication of those of lichen planus. There were no lesions on the buccal mucosa.

One of the bullous lesions was examined histologically; it exhibited the characteristic features of bullous lichen planus.

DISCUSSION

DR. HOWARD FOX: The case is an interesting one on account of the age of the child. It is well known, however, that lichen planus, while uncommon in children, has been noted in persons at all ages from 1 year up.

DR. E. F. TRAUB: I would like to ask Dr. Wise about the vesicular or bullous lesions on the face and whether the possibility of epidermolysis bullosa has been ruled out. Some of the lesions on the hands and arms had the appearance of epidermal inclusion cysts rather than of lichen planus.

DR. P. E. BECHET: I saw more than one vesicle with perfectly clear serum; the vesicle was much deeper than those usually found in generalized impetigo. It seems to me that children are unusually prone to have vesiculobullous lesions, certainly more so than adults. This is true in urticaria, lichen planus and other dermatoses. It would be interesting to speculate on the cause of this phenomenon.

SCLERODERMA OF GENERALIZED PROGRESSIVE TYPE. Presented by DR. HOWARD FOX.

M. S., a stone cutter, aged 53, first noticed cutaneous changes thirteen months previous to presentation. At the outset there were swelling and stiffness of the backs of the hands, which were present until six months prior to presentation.

The arms then became involved and later the face, trunk and legs. During the past few months the patient had noticed difficulty in breathing, due to limitation in expansion of the chest. The skin on the face, trunk and upper extremities was smooth, shiny and hidebound; that on the lower extremities was similarly but much less markedly affected. There were diffuse areas of light brownish pigmentation. There was no disturbance of sweating. The hair was normally oily. There was some limitation of motion of the elbow and interphalangeal joints. The thyroid gland could not be palpated.

The patient had recently been under observation at the Presbyterian Hospital, where the following data were supplied by Dr. J. Gardiner Hopkins. The patient was discharged from the hospital with the diagnosis of chronic pulmonary tuberculosis, moderately advanced and quiescent, calcification of mesenteric lymph glands, pneumonoconiosis, and scleroderma. There were moderate dulness over the apexes of the lungs, dulness over the lower right lobe with increased fremitus, exaggerated voice sounds and râles and occasional friction sounds. Roentgen examination of the chest showed very slight changes, interpreted as pulmonary tuberculosis. These changes were thought to be possibly silicosis, as the man had been a stone cutter. Seven examinations of the sputum for tubercle bacilli gave negative results. There were no changes in the bones of the hands on roentgen examination. Roentgenograms of the paranasal sinus showed slight clouding. The Wassermann test was negative; the blood count was essentially normal. The basal metabolic rate varied from plus four to plus nine.

DISCUSSION

DR. P. E. BECHET: I presented this patient at the last meeting of the Academy, and I also was impressed by the extensive character of the eruption and its rapid progress.

DR. FRED WISE: I had a patient with a condition similar to this; I sent him to the Mayo Clinic for a spinal gangliectomy. Six weeks following the operation the scleroderma was markedly improved.

DR. GEORGE M. MACKEE: In the literature there are reports of cures effected by medical diathermy and also by roentgen rays applied both to the affected skin and to the spinal column.

DR. J. E. LANE: I have had a patient with a case of five or six years' duration whose condition improved markedly under treatment with massage and cod liver oil. It is unusual to obtain great improvement with widespread lesions.

DR. FRED WISE: The patient to whom I referred had received all the treatment that has been mentioned—massage, diathermy, etc.—and he showed no improvement until after the spinal gangliectomy.

PITYRIASIS RUBRA PILARIS IN A CHILD AGED THREE. Presented by DR. P. E. BECHET.

M. V., a girl, aged 3 years, for four weeks had fine acuminate, slightly keratotic papules scattered over the body. On the left leg these papules had aggregated to form large bright red patches, with the characteristic dry hyperkeratotic surface. There was marked keratosis of the palms and soles. The patient was presented because of the unusually early incidence of the disease.

DISCUSSION

DR. E. F. TRAUB: Certainly the clinical appearance of this eruption is that of a typical pityriasis rubra pilaris. While I was speaking to the parents, however, they stated that the child had taken some medicine for whooping cough, immediately following which the eruption on the body had appeared. I should like to ask Dr. Bechet whether this factor has been considered.

DR. F. C. COMBES: Irrespective of the fact that medicine may have been administered before the outbreak, I agree with the diagnosis.

DR. HOWARD FOX: The patient is young to have this disease, but it occurs in children as young as she. The eruption seems typical, particularly the hyperkeratosis of the palms.

DR. P. E. BECHET: The child presents the typical and graphic picture of the disease. Palmar and plantar keratoses, individual, fine, acuminate keratotic papules, and bright red, dry, hyperkeratotic patches are present. Certainly such a picture does not fit in with the diagnosis of rash due to a drug, even if the child had taken a drug, which the mother denied.

LICHEN PLANUS LINEARIS. Presented by DR. E. R. MALONEY.

C. D., a colored girl, aged 8 years, presented an eruption of eight weeks' duration consisting of closely packed, small, shiny papules. There was a patch of papules on the right side of the upper part of the chest about 2 inches (5.08 cm.) square; from this patch a line of papules ran across the chest to the anterior surface of the shoulder and thence down the anterior surface of the arm.

DISCUSSION

DR. FRED WISE: I think that the case is one of nevus tardus. Cases of this kind in which the nevus tardus is like lichen planus have been frequently described. Such a case was described by Ketron, among others.

DR. GEORGE M. MACKEE: As so often happens, it is extremely difficult definitely to settle the question of the identity of the disease or condition in this case. Lichen planus may resemble a linear nevus, or vice versa. The histology is often confusing. The history may not help much, because nevi may become visible long after birth. Clinically this is a case of linear lichen planus; I prefer to wait until after the tissue has been studied histologically before making more than a tentative diagnosis. Treatment may not help much in establishing the diagnosis, because linear lichen planus and linear psoriasis are likely to resist treatment, as does linear nevus. Histologic examination may or may not establish a diagnosis; it will probably do so.

DR. J. F. FRASER: Is it not a fact that lesions that are distinctly typical of linear nevus may show a histologic picture resembling that of lichen planus?

DR. FRED WISE: It is my experience that in a case of this kind the condition does not respond to treatment with roentgen rays.

DR. E. F. TRAUB: Last fall I presented before this society a case similar to this one, except that the eruption was more extensive, involving entirely one side of the body. The question of whether the case should be called one of linear lichen planus or of nevus linearis was discussed and was not settled conclusively, even following the microscopic examination, which also apparently favored the diagnosis of lichen planus. The patient had received both roentgen and radium treatments to the extent of having received a severe third degree burn for which plastic repair had to be instituted. Nevertheless, at the margin of the overtreated areas where actual total destruction has not taken place, active lesions of the process were still present. Therefore, I agree that the patient presented is not likely to respond to any type of radiation, and in that sense the process more nearly resembles a nevus.

DR. GEORGE M. MACKEE: An analogous condition is lichen planus following the administration of arsenic. In such cases, in which both clinically and histologically the eruption is lichen planus, the diagnosis of lichen planus must be made. Then one can say that lichen planus occurred coincidentaly with the administration of arsenic; that arsenic precipitated an attack of lichen planus, or that arsenic may produce an eruption independent of lichen planus. In this connection, it may be recalled that arsenic is said to cause zoster. Zoster is an exceedingly common affection, and the fact that occasionally it follows the administration of arsenic is not a good reason for believing that arsenic is the cause, though, of course, it may be.

DR. W. J. HIGHMAN: In a discussion like this the situation is embarrassing as to the standards by which one groups diseases of the skin. If this condition is lichen planus, as Dr. Maloney thinks, this much may be said favoring the view: The child was not born with the eruption. If it had been born with it and nevertheless the structure of lichen planus were found microscopically, a congenital anomaly of the skin presenting the structure of lichen planus would be present. If a child from 4 to 5 years of age has an acquired eruption that is histologically lichen planus, there is no reason to call it a retarded nevus. The only reason to suspect nevus is the peculiar distribution, but I should want to see the nevus under the microscope. If the condition can be demonstrated to be lichen, the whole case for linear nevus falls.

DR. E. R. MALONEY: Of course, the diagnosis of linear nevus was considered, but the duration of the disease and the characteristic papules seem to be sufficient to warrant the diagnosis of linear lichen planus.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. FRED WISE.

Mrs. A. F., aged 32, a patient referred by Dr. Strauss of New Haven, who was first examined at the Post-Graduate Hospital on Oct. 1, 1931, gave a history of having had a cutaneous eruption for eight months. It began as an erythematous rash on the chest, which spread and began to involve other areas. At the time of the first examination there was an eruption confined to the V of the neck, consisting of fairly sharply demarcated, scaling and erythematous patches arranged in a roughly reticular formation. There was no sharp demarcation between the affected areas and the normal skin, and there was no definite atrophy, though some of the lesions seemed to be healing, leaving a somewhat thin epidermis. On the extensor surfaces of both forearms and on the elbows, sharply circumscribed scaling and erythematous patches were seen. These patches were irregular and in some ways resembled the lesions of parapsoriasis en plaques, except that there was telangiectasia, and that the scaling was more white. On the dorsa of the fingers there were sharply demarcated, irregular patches of a bizarre shape which were clinically typical of lupus erythematosus, presenting the slightly bluish color and the follicular scaling as well as an indication of atrophy in some of the healing areas. The cheeks showed the lesions of erythema perstans faciei.

General examination of the patient gave negative results, with the exception of profuse swelling of the joints of the hands and wrists and signs of myocarditis. (Dr. Arthur Fishberg made a diagnosis of Libman-Sachs syndrome.)

Treatment consisted of the administration of antipruritic remedies, as the eruption itched, and plasmochin given by mouth. Through an oversight, the patient took three times the normal maximum dose of plasmochin, and on September 9 she became acutely ill and had to go to bed. A new eruption appeared at this time, consisting of large bullae, approximately round and from 2 to 3 inches (5.08 to 7.62 cm.) in diameter, which developed suddenly on an unaffected base. One lesion was present on the forehead, one on the right side of the chin immediately below the lip, one on the right elbow, and one on the back of the neck. When the bullae burst, the affected areas were covered with serosanguineous crusts. The mucous membranes were unaffected. There were diarrhea, elevation of temperature up to 102 F. and a rapid pulse rate of 120. Otherwise she was normal, and the original eruption seemed to have faded somewhat.

The bullous eruption disappeared, and the patient's general condition became rapidly normal under the discontinuance of the plasmochin and the forced administration of fluids. A diagnosis of bullous eruption due to plasmochin was made.

DISCUSSION

DR. GEORGE M. MACKEE: Dr. Wise wished to have a discussion regarding the value of gold preparations in this case. I think that we agree that the use of gold compounds is not very effective in the disseminated type of this condition

and that such drugs must be used with caution. When a patient seems to be highly sensitized to gold, as does the one presented, it would seem preferable to avoid it entirely.

DR. JEROME KINGSBURY: I agree with Dr. MacKee that this case is not suitable for therapy with gold preparations.

DR. P. E. BECHET: In view of the acute symptoms, it might be advisable to use exceedingly small doses of a gold compound or perhaps not to use it at all. On the other hand, I recall a most extensive and acute case of lupus erythematosus with lesions on the chest, arms, hands and face. The patient had lost 30 pounds (13.6 Kg.) in a few weeks, had constitutional symptoms and seemed seriously ill. This was in the early days of aurotherapy, when little or nothing was known about the contraindications; hence injections of gold protein sent to me by Dr. Schamberg were given in fairly large doses. The dosage used was much larger than it is today. Every injection was followed by a severe protein reaction within the hour of its administration; yet despite this the results were almost miraculous. The patient made a rapid and complete recovery. If we had feared to employ the treatment and had not made use of it the patient would undoubtedly have died of a generalized toxemia as the result of the disseminate lupus erythematosus.

DR. W. J. HIGHMAN: In the situation in which Dr. Wise finds himself, would it not be wise to try the old-fashioned Hollander treatment?

LICHEN PLANUS HYPERTROPHICUS (RESULTS OF TREATMENT). Presented by DR. PAUL E. BECHET.

E. F., a woman, aged 33, stated that two years previously an eruption had appeared on the arms and legs, which on inspection proved to be papular lichen planus on the arms and hypertrophic lichen on the legs. The lesions on the legs consisted of large raised, verrucous, hypertrophic nodules, from 2 to 3 mm. in diameter; there were many scratch marks. The lesions were very pruritic. About a year and a half previously she had received irradiation with seven and a half quarter unit doses of roentgen rays on the legs, once a week, without appreciable benefit. One year later the eruption had not changed. A salve containing phenol and corrosive mercuric chloride ointment of lead oleate, U. S. P., sufficiently strong to cause a repeated dermatitis was then given. No medication had been used during several weeks prior to presentation, and the patient exhibited perfectly flat, pigmented areas; the nodules had almost entirely disappeared. This beneficial effect had been noted even after the first week of application.

The patient was presented because of the negative results obtained by roentgenotherapy and the splendid results obtained by the use of an old, tried and useful application, now completely and inadvisedly outmoded.

HEREDITARY ESSENTIAL TELANGIECTASIA. Presented by DR. FRED WISE.

In Mrs. L., a woman, aged 27, a patient referred by Dr. Wright of the Post-Graduate Hospital, whose general health was good, with the exception of a susceptibility to pernios of the hands and feet, tests for syphilis and tuberculosis were negative. The patient had had one pregnancy which resulted in a stillbirth. Necropsy revealed that the baby presented multiple hemorrhages in all of the viscera. The mother exhibited a widely disseminated and diffuse bluish-red to violaceous discoloration of the entire lower extremities, extending actively toward the groins and buttocks. The process appeared to spread during the few months that the patient was under observation.

Examination of the skin revealed a fine network of superficial capillaries, without evidence of hemorrhage or ring formation, which disappeared partly on diascopic pressure. There was no pigmentation.

Treatment with intensive ultraviolet irradiation had apparently not improved the condition up to the time of presentation.

DISCUSSION

DR. C. M. WILLIAMS: This is an interesting and difficult case. Without the history the clinical appearance is that of essential telangiectasia, a congenital weakness of the walls of the blood vessels, resulting in dilatation and, sometimes, hemorrhages. Such cases resemble cutis marmorata caused by lead, but they may occur without discoverable cause. In other cases, similar symptoms may be the result of syphilitic or tuberculous inflammation in or around the deeper vessels.

The death of a child of the patient who showed at autopsy hemorrhages of the internal organs suggests a diagnosis of hereditary hemorrhagic telangiectasia, but in this disease hemorrhages usually occur from the superficial mucous membranes and the telangiectasias usually appear on the exposed parts. The disease is common and often overlooked, because the symptoms may be very mild; often the hemorrhages occur in one member of a family, while the telangiectasias are observed in another, and many of the children escape entirely.

DR. HOWARD FOX: Since Dr. Williams called our attention to the subject, I have made a point of including in the history of every such patient a statement as to whether or not he had suffered from nosebleed. Thus far I have not been able to find a patient who had suffered from nosebleed.

DR. W. J. HIGHMAN: One phase of Dr. Williams' discussion should be emphasized, that of telangiectasis due to syphilis. The most important contribution to the subject in this country was made by Stokes, and shortly after its appearance I had a patient who complained of telangiectasis of the back. So far as she knew she had not had syphilis; but there was a strongly positive Wassermann reaction, and under antisyphilitic treatment the telangiectasis disappeared. In Dr. Wise's case the Wassermann test is negative, and yet it is possible that the patient has syphilis. For this reason, I think that a therapeutic test should be made to see whether the capillary disturbance will clear up. It is worth trying.

DR. FRED WISE: I shall be glad to transmit Dr. Highman's suggestion to Dr. Wright.

SCLERODERMA EN BANDE. Presented by DR. FRED WISE.

The patient, a girl, aged 14, who had previously been presented before the Manhattan Dermatological Society, exhibited a band of indurated, stiff, bound-down, waxy-yellow skin about an inch (2.5 cm.) broad and six inches (15.2 cm.) long, extending from the lobe of the left ear in a diagonal line down to the clavicle. In the center of this band there was a morphea-like roughly circular plaque of increased hardness and firmness, with a diameter about that of a twenty-five cent piece. The edges of the band showed a narrow zone of inflammatory reaction.

DISCUSSION

DR. HOWARD FOX: I saw this patient two or three years ago, and do not think any change has occurred in the morphea since then. I should like to ask whether any one present has ever followed a case of morphea and seen it disappear.

DR. GEORGE M. MACKEE: Yes, I have seen one slowly disappear spontaneously, leaving atrophy.

DR. C. M. WILLIAMS: I know of a case that ended in death.

DERMATITIS PAPILLARIS CAPILLITII — KELOIDS. Presented by DR. E. F. TRAUB.

J. B., a colored man, 34 years of age, married (from the Stuyvesant Square Hospital, formerly the Skin and Cancer Hospital), stated that the condition began as a small "pimple" on the back of the neck three years previously. He stated further that six months after the onset of the present condition he had taken

bromides for a short period of time because of a nervous ailment. The process extended rapidly, involving the entire back of the neck, patchy areas of the scalp and the bearded region of the face. As presented, there was a large keloidal mass in the center of the nape of the neck, measuring from 2½ to 3 inches (6.3 to 7.6 cm.) in diameter and in places discharging a watery purulent material, particularly about some included and infected hairs. The other lesions about the neck were much smaller, varying in size from several millimeters to about 2 cm. All of the lesions were located about infected hairs, and free pus was obtainable from most of them. Similar lesions were found in the bearded region of the face and in patches about the scalp, and about each lesion in the scalp was a small area of alopecia.

DISCUSSION

DR. GEORGE M. MACKEE: I think that the lesion can be cured by surgical diathermy, with the cutting current applied by means of a wire loop electrode; the lesion should be shaved down to the level of the normal skin and then postoperative treatment with roentgen rays given. This treatment will not absolutely prevent recurrence, but it will do so in a majority of instances. So far as roentgen technic is concerned, a fractional treatment may be given once a week or a suberythema dose once a month. In either case, several months will be required for cure.

DR. W. J. HIGHMAN: A striking point about this patient is that he is too old to have ordinary acne, which he has on his face. He does not have the kind of neck on which dermatitis papillaris is usually seen.

DR. E. F. TRAUB: The history I obtained concerning bromides was that the eruption had started six months before this drug was used, and apparently so far as the patient could tell, the process seemed little affected by ingestion of the medicine. I should like to ask Dr. MacKee what his experience has been in the management of this type of case with roentgen therapy and also with the use of the electric cutting current.

DR. GEORGE M. MACKEE: Treatment with the electric cutting current can be given quickly under local anesthesia with procaine hydrochloride, only a few minutes being required. The method is much more rapid than removal with the needle electrode, and the end-result is better. Such treatment is likely to leave a depigmented scar (in the skin of Negroes), but this discoloration can easily be camouflaged with a suitable stain.

DR. E. F. TRAUB: I am interested to hear how Dr. MacKee treats this type of patient, as we have had a number of them in our roentgen ray clinic. In most instances in which less than a skin unit dose of roentgen rays is used, practically no response to treatment occurs, and in the cases in which as much as a full skin unit is given once a month, only slight improvement is noted. The best results were obtained in cases in which we combined curettement or removal of the masses with either fulguration or the electric cutting current, immediately followed by the administration of skin unit doses of roentgen rays to prevent their regrowth.

EXCORIATIONS OF BUCCAL MUCOSA (?). Presented by DR. F. C. COMBES.

J. S., a boy, aged 15 years, presented many excoriations and maceration of the buccal mucosa. The condition was of eight months' duration. The patient gave a history of more or less constant biting of the mucosa with his teeth. The case had been referred to the skin department of the University and Bellevue Medical College by the Dental School, where exhaustive bacteriologic and mycologic examinations had yielded no results. The histologic examination was unsatisfactory, and the condition was reported as epithelial hyperplasia. The purpose of the presentation was to exclude the diagnosis of a disease process of the mouth.

DISCUSSION

DR. GEORGE M. MACKEE: The lesions do not resemble excoriations. The condition resembles rather a definite eruption, a disease. My first thought, despite results of the bacteriologic examination, would be that the condition is a yeast dermatitis. I should want that possibility ruled out before any other possibility is considered. A therapeutic test might help, for some of these cases of stomatitis respond well to treatment with iodine. Various other conditions such as lichen planus, Vincent's angina and possibly lupus erythematosus should be considered.

DR. F. C. COMBES: I appreciate Dr. MacKee's discussion. The bacteriologic examination was complete, and only one yeastlike cell was found in all of the examinations. The lesions were very smooth to the touch, and they did not have the feel of leukoplakia.

NEVUS FLAMMEUS OF ARM AND HAND, ASSOCIATED WITH FIBROSIS AND PYOGENIC GRANULOMAS. Presented by DR. FRED WISE.

W. M., a man, aged 52, was first seen at the Post-Graduate Clinic on Nov. 21, 1931. He presented an extensive nevus flammeus which involved the skin of the right hand, forearm and arm, up to the shoulder. There was also a large port-wine mark extending from the right scapular area to the right nipple in a band 3 inches broad. The nevus of the arm was thickly studded with elevated angiomatous and fibromatous papules of various colors varying from flesh pink to violaceous and ranging in size from that of a pinhead to that of a pea. On the back of the right hand, between the middle and the ring fingers, there was a pedunculated lesion about the size of a small hazelnut, the surface of which was bathed in pus and a sanguineous fluid. The lesion seemed to spring from the midst of the vascular tissue as though it were a part of the angioma. The lesion was of two and a half months' duration.

Histologic examination revealed a typical pyogenic granuloma.

DISCUSSION

DR. W. J. HIGHMAN: Of course, this condition is either a granuloma pyogenicum or a neoplasm, and there are reasons for both points of view. The smaller lesion has no pedunculated attachment. Even neoplasms may be pedunculated. Dr. Williams spoke of this fact while the patient was being presented. The pedunculation of the larger lesion is more of the mushroom style. I should be better satisfied to make a diagnosis after seeing a microscopic specimen.

DR. E. F. TRAUB: In association with this type of vascular nevus one frequently sees multiple fibromas. Ordinarily, of course, they do not bleed or have a pedunculated base, but owing to the peculiar location of the lesions in this instance it might be worth while to consider the possibility of a fibroma as the diagnosis in this case.

DR. GEORGE M. MACKEE: There are two types of pyogenic granuloma; one of them is distinctly pedunculated and the other is not. The lesions that are not pedunculated simulate a rapidly growing sarcoma. I think that this patient has both types of lesions, pedunculated and nonpedunculated. In this case the diagnosis is based on the pedunculation of one tumor, on the ease with which it bleeds on slight traumatism, and also on the slimy discharge almost constantly present.

DR. JOHN E. LANE: On the smooth surface a granuloma pyogenicum does not usually discharge much pus. In this case there is a good deal of pus. This is probably due to the location, as one finger rubbed against the other and produced maceration and another infection.

DR. J. F. FRASER: I think that the points referred to by Dr. Highman and Dr. MacKee are well taken. There is a possibility that this lesion may be a melanoma. I should suggest that one of these growths be excised and examined microscopically.

DR. W. J. HIGHMAN: Has the patient any enlarged axillary lymph glands?

DR. WISE: No.

PEMPHIGUS. Presented by DR. E. F. TRAUB.

H. D., a valet, aged 58, married, born in England, stated that about three months previously he noticed a small eruption on the glans penis. This condition failed to heal under local protective treatment and gradually spread, involving the entire glans penis and the adjacent skin. At the onset it was difficult to be certain whether the eruption was a dry scaly condition or whether the lesions were dried crusts. With the view that the condition might be localized psoriasis, several small fractional doses of roentgen rays were administered, without benefit. About two months prior to presentation, small, flat, definitely rounded lesions appeared on the scrotum. At first, only one or two discrete lesions with normal skin between them were found to be present, but this number had gradually increased so that when the patient was presented there were from twelve to fifteen such patches. The lesion on the glans penis had become definitely moist, and the entire process seemed to be made up of bullae in which crusting developed so rapidly that the true nature was not readily determined. The Wassermann test of the blood was negative. Other laboratory data were not available.

DISCUSSION

DR. GEORGE M. MACKEE: Of course, I realize that an eruption of this kind may be pemphigus, but one must consider the possibilities of dermatitis venenata due to a contraceptive, an eruption due to drugs and even psoriasis. I suggest that a phytopharmacologic test be made.

DR. W. J. HIGHMAN: Dr. MacKee has stated the case perfectly. The floor of the lesion on the glans, with its puckered surface, is seen in psoriasis after a scale is removed. Yet there is no strong evidence of psoriasis; there is too much exudation.

DR. C. M. WILLIAMS: So far the discussion has centered on the lesions on the glans, but there are others on the scrotum that could hardly be caused by an external irritant. These scrotal lesions are round, from 1 to 3 cm. in diameter, sharply outlined, inflammatory, and separated from each other by normal skin. They are too discrete to be caused by an irritant and too moist to be caused by psoriasis. The scales consist partly of dried exudate. The case reminds me of one seen at the Skin and Cancer Hospital several years ago, in which there were lesions in the groins and on the scrotum, and some, I believe, in the axillae. Various diagnoses were made, such as intertrigo, tinea cruris, psoriasis, etc. Cultures and microscopic examinations were inconclusive. Finally the lesions vegetated, and the man died of pemphigus.

DR. E. F. TRAUB: I hesitated for some time before bringing this patient before the society, because I felt that a great many of the members would not accept a diagnosis of pemphigus without the presence of a widespread typical bullous eruption with an obviously fatal outlook. I have now followed the case long enough to be in position to definitely rule out psoriasis, as the patient has no other symptom or history of the condition and the local lesions no longer suggest it. As Dr. Williams pointed out, a dermatitis venenata producing discrete patches with healthy skin between them, as seen on the patient's scrotum, is highly improbable. Though it may not materially help in preventing a fatal outcome, nevertheless an early diagnosis of this disease will certainly give us a better chance to help the patient than to wait patiently until the skin is hopelessly involved.

CARCINOMA OF BUCCAL MUCOSA OF LEFT CHEEK. Presented by DR. FRED WISE.

S. C., a man, aged 56, applied for treatment at the Post-Graduate Clinic on Nov. 24, 1931. On the inner side of the left cheek, just behind the angle of the mouth, there was a firm mass the size of a pigeon's egg. The surface was smooth

and inflamed but not ulcerated. For many years the patient had been in the habit of smoking a pipe, the stem of which rested against the affected area. Seven or eight months prior to his visit to the clinic, he had noticed a small lump in his mouth; this had steadily increased in size but had caused no discomfort. The Wassermann and Kahn tests of the blood were negative. Biopsy revealed a transitional cell type of carcinoma, with a slight degree of cornification.

NOTE.—The tumor was subsequently removed by bipolar electrocoagulation, and filtered roentgen rays were applied to the glands of the neck, which, however, were not enlarged.

DISCUSSION

DR. GEORGE M. MACKEE: This case is very unfavorable and it is probably hopeless, but we should not assume this. Therapeutically, one should do the best one can. There are several angles of approach. Without mentioning all of the therapeutic methods that could be used, I should prefer thoroughly to coagulate the entire lesion and a portion of the surrounding healthy tissue. By using a bipolar electrode with two prongs about 2 mm. apart, a strong current can be employed without giving the patient a shock, and with multiple insertions of the bipolar electrode it would be possible to coagulate the entire growth. The coagulated mass is then removed with the cutting current. After this is done, it might be well to employ gold radon seeds in large doses, with from 1½ to 2 millicuries of radon in each seed. The seeds are placed in and around the lesion, 1 cm. apart. This procedure would produce a painful reaction, which could be greatly lessened by a suitable denture made by a dentist. A suitable denture prevents the occurrence of dermatitis of the entire mouth. The denture is made with a dental molding compound to fit the mouth; lead or zinc is then inserted in the molding compound, which absorbs the secondary rays so that dermatitis due to secondary rays is prevented; the lead absorbs the gamma rays that would otherwise affect the entire mouth. In addition, heavily filtered high voltage roentgen radiation should be applied to the neck.

Book Reviews

Ekzema infantum und Dermatitis seborrhoides. By Ernest Moro, Professor of Pediatrics, University of Heidelberg. Price, $5.75. Pp. 170. Berlin: Julius Springer, 1932.

This is an excellent work by a pediatrician on the subject of infantile eczema and allied dermatoses. The first section of 50 pages is devoted to clinical considerations, with case reports and photographic illustrations of intertriginous dermatitis, seborrheic dermatitis, psoriatic dermatitis, erythroderma, erythroderma desquamativa of Leiner and the various clinical types of eczema. These dermatoses are lucidly presented and differentiated in an original manner, and the subjects of crusta lactea, erythroderma desquamativa of Leiner and neurodermatitis are particularly well discussed.

In the next section of 120 pages on pathogenesis, more than 50 pages are devoted to the consideration of infantile eczema as an allergic phenomenon, with alimentary allergy predominant, and the important antigens are discussed.

Eczema is also considered at times a vasomotor reflex neurosis activated by local external irritation, and at times as the exhibition of a diathesis, a nutritional disturbance or a metabolic disorder. The tendency to diffuse erythematous dermatitis and desquamation and to seborrheic features is attributed to the anatomic and physiologic characteristics of infantile skin. Importance is attached to the site and the soil in which eczematoid reactions develop, and these reactions are differentiated as of three types: the seborrheic, the lymphophile and the angioneurotic, or combinations of these.

Seborrheic dermatitis is definitely dissociated from the eczema group, and considerable speculation is given to a consideration of its pathogenesis and etiology. While no special attention is devoted to therapy, the underlying principles on which intelligent treatment should be based are to be found in the comments on pathogenesis.

The author does not lose sight of practical considerations and repeatedly inserts brief, well illustrated case references.

Fundamentals of Dermatology. By Alfred Schalek, Professor of Dermatology and Syphilology, University of Nebraska. Second edition. Price, $3. Pp. 246, with 58 illustrations. Philadelphia: Lea & Febiger, 1931.

This book is really not a treatise on the fundamentals of dermatology but a synopsis of dermatology, and is a good example of this sort of manual. It gives accurately, but in bare outline, the pictures of cutaneous diseases, and its usefulness, like all such manuals, must be chiefly in diagnosis. One cannot get an intelligent picture of any cutaneous disease from so brief a description, and such a book must be supplemented by a larger work to which the puzzled reader may refer after he thinks he has located the disease in which he is at the moment interested. Schalek has done his job well, but the question must be raised as to the value of such brief synopses, except perhaps in cramming for an examination.

Directory of Dermatologic Societies *

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

George Miller MacKee, Chairman, 200 W. 59th St., New York.
Francis E. Senear, Secretary, 55 E. Washington St., Chicago.
Place: New Orleans. Time: May 9-13, 1932.

American Dermatological Association

W. H. Mook, President, 3720 Washington Blvd., St. Louis.
W. H. Guy, Secretary, 7026 Jenkins Arcade, Pittsburgh.
Place: Havana, Cuba. Time: May 3-5, 1932.

British Association of Dermatology and Syphilology (Canadian Branch)

Philip Burnett, President, 2 Simpson St., Montreal.
L. P. Ereaux, Secretary, 1380 Sherbrooke West, Montreal.
Place: Toronto. Time: June 24, 1932.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Lee McCarthy, President, 1835 Eye St. N. W., Washington, D. C.
M. H. Goodman, Secretary, 401 Medical Arts Bldg., Baltimore.

Central States Dermatological Association

Howard J. Parkhurst, President, 316 Michigan St., Toledo, Ohio.
Robert E. Barney, Secretary, 1021 Prospect Ave., Cleveland.
Place: Pittsburgh. Time: October, 1932.

Iowa and Western Illinois Dermatological Association

J. C. Kessler, President, University Hospital, Iowa City.
J. W. Bailey, Secretary, 10th St., and Grand Ave., Des Moines, Iowa.

New England Dermatological Society

Arthur M. Greenwood, President, 416 Marlboro St., Boston.
William P. Boardman, Secretary, 388 Marlboro St., Boston.

Southern Medical Association, Section on Dermatology

Emmet R. Hall, Chairman, 1001 Exchange Bldg., Memphis, Tenn.
Dudley C. Smith, Secretary, University, Va.

STATE DERMATOLOGIC SOCIETIES

Louisiana Dermatological Society

R. A. Oriol, President, 921 Canal St., New Orleans.
M. T. Van Studdiford, Secretary-Treasurer, 150 Baronne St., New Orleans.

---

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Edward R. Maloney, Chairman, 853 7th Ave., New York.
George C. Andrews, Secretary, 115 E. 61st St., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA SECTION ON DERMATOLOGY

Edward F. Corson, President, Medical Arts Bldg., Philadelphia.
Stanley Crawford, Secretary, 200, 9th St., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Cyril K. Valade, Chairman, 1604 Eaton Tower, Detroit.
George H. Belote, Secretary, University Hospital, Ann Arbor.

MINNESOTA DERMATOLOGICAL SOCIETY

H. N. Klein, President, 350 St. Peter St., St. Paul.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.

OKLAHOMA DERMATOLOGICAL ASSOCIATION

C. J. Woods, President, 108 W. 6th St., Tulsa.
C. L. Brundage, Secretary, 616 Medical Arts Bldg., Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

N. Riley Jackson, President, 110 W. 7th St., Austin.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.

LOCAL DERMATOLOGIC SOCIETIES

ATLANTA DERMATOLOGICAL SOCIETY

Francis G. Jones, President, 384 Peachtree St., Atlanta, Ga.
Charles A. Wilkins, Secretary, Medical Arts Bldg., Atlanta, Ga.

BRONX DERMATOLOGICAL SOCIETY

Henry Silver, Chairman, 290 West End Ave., New York.
Theodore Rosenthal, Secretary-Treasurer, 115 W. 86th St., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

A. M. Persky, Secretary, 1750 Ocean Pkwy., Brooklyn.
B. B. Berkowitz, President, 225 Eastern Parkway, Brooklyn.

CHICAGO DERMATOLOGICAL SOCIETY

Michael Ebert, President, 25 E. Washington St., Chicago.
E. A. Oliver, Secretary, 55 E. Washington St., Chicago.

CINCINNATI DERMATOLOGICAL SOCIETY

H. Jerry Lavender, President, 716 Provident Bank Bldg., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

CLEVELAND DERMATOLOGICAL SOCIETY

Howard J. Parkhurst, President, 316 Michigan St., Toledo.
Robert E. Barney, Secretary, 1021 Prospect Ave., Cleveland.

Detroit Dermatological Society

Claud W. Behn, President, 1546 David Whitney Bldg., Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.

Los Angeles Dermatological Society

Irving R. Bancroft, Chairman, 412 W. 6th St., Los Angeles.
Chris R. Halloran, Secretary, 1052 W. 6th St., Los Angeles.

Manhattan Dermatologic Society

George Miller MacKee, Chairman, 200 W. 59th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

Montreal Dermatological Society

Philip Burnett, President, 2 Simpson St., Montreal.
Lemuel P. Ereaux, Secretary-Treasurer, 1390 Sherbrooke St., West, Montreal.

New York Academy of Medicine, Section of Dermatology and Syphilis

Joseph J. Eller, Chairman, 100 W. 59th St., New York.
Leo Spiegel, Secretary, 241 W. 100th St., New York.

New York Dermatological Society

John Frank Fraser, President, 100 W. 59th St., New York.
Edward R. Maloney, Secretary, 853 7th Ave., New York.

Philadelphia Dermatological Society

Jacob M. Schildkraut, Chairman, 170 W. State St., Trenton, N. J.
Jacques P. Guequierre, Secretary, 1930 Chestnut St., Philadelphia.

Pittsburgh Dermatological Society

J. H. Fiscus, Chairman, 121 N. Main St., Greensburg, Pa.
Claude B. Norris, Secretary, 244 Lincoln Ave., Youngstown, Ohio.
Place: Pittsburgh. Time: October, 1932.

St. Louis Dermatological Society

Richard S. Weiss, President, 3720 Washington Blvd., St. Louis.
M. F. Engman, Jr., Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

San Francisco Dermatological Society

Charles Schoff, President, 1127, 11th St., Sacramento, Calif.
John M. Graves, Secretary, 909 Hyde St., San Francisco.

Index to Current Literature

DERMATOLOGY

Actinic Ray Therapy of Malignant Neoplasms of Tongue and Jaw. A. Zieszyński and E. Meisels, Polska gaz. lek. **10**:983 (Dec. 20) 1931; abstr., J. A. M. A. **98**:860 (March 5) 1932.

Acute Generalized, Cutaneous, Miliary Tuberculosis During Childhood. E. Nedelmann, Jahrb. f. Kinderh. **134**:24 (Dec.) 1931.

An Investigation into Streptococci Found in Certain Diseases of Skin. J. Kinnear, Brit. J. Exper. Path. **12**:384 (Dec.) 1931.

Behavior of Capillaries and of Cutaneous Glands During Diseases of Blood. E. Jurgensen, Deutsches Arch. f. klin. Med. **172**:233 (Dec. 21) 1931.

Bismuth Agranulocytosis. A. Sezary and G. Boucher, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:1795 (Dec. 7) 1931.

Carbon Tetrachloride in Treatment of Taenia Infections. P. A. Maplestone and A. K. Mukerji, Indian M. Gaz. **66**:667 (Dec.) 1931.

Chronic Paragenital Serpiginous Soft Chancre: Case. L. I. Yudovich and E. P. Malkovskaya, Sovetskaya med. vostochnoy sibiri, Jan.-Feb., 1931, p. 104.

Clinical Aspect and Etiology of Sarcoid of Boeck. A. Kissmeyer, Hospitalstid. **74**:1047 (Nov. 5) 1931; abstr., J. A. M. A. **98**:1126 (March 26) 1932.

Concept of Dosage and Definition of r Unit (Roentgen Unit). R. Glocker, Radiology **18**:93 (Jan.) 1932.

Congenital Cysts and Fistulas of Neck. H. W. Meyer, Ann. Surg. **95**:1 (Jan.) 1932.

Development of Dermatology to Its Present Status: Consideration of Its Contribution to Internal Medicine. C. B. Willmott, South. M. J. **25**:63 (Jan.) 1932.

Diagnosis and Treatment of Cancer of Skin. M. D. Ratcliff, New Orleans M. & S. J. **84**:550 (Jan.) 1932.

Epicutaneous Tuberculin Reaction in Tuberculosis of Skin. E. Nathan and P. Kallós, Klin. Wchnschr. **10**:2392 (Dec. 26) 1931.

Epidemic of Chickenpox with Herpes Zoster. P. J. Braslawsky, Presse méd. **39**:1671 (Nov. 14) 1931.

Epileptic Convulsions of Dementia Paralytica: Their Relation to Sclerosis of Cornu Ammonis. H. H. Merritt, Arch. Neurol. & Psychiat. **27**:138 (Jan.) 1932; abstr., J. A. M. A. **98**:920 (March 12) 1932.

Erysipeloid: Transmission of Swine Erysipelas to Man. G. Belgodere, Ann. de dermat. et syph. **2**:1241 (Dec.) 1931; abstr., J. A. M. A. **98**:927 (March 12) 1932.

Erythredema or Pink Disease. G. Willcocks, Practitioner **128**:87 (Jan.) 1932.

Established Actinotherapeutic Modalities in Dermatology. M. Scholtz, Arch. Physical Therapy **13**:28 (Jan.) 1932.

Experimental Study of Case of Herpes Recurrens. N. N. Klodnitskiy, Sovetskaya med. vostochnoy sibiri, Jan.-Feb., 1931, p. 71; abstr., J. A. M. A. **98**:932 (March 12) 1932.

Gangrene in an Infant, Associated with Temporary Diabetes. R. D. Lawrence and R. A. McCance, Arch. Dis. Childhood **6**:343 (Dec.) 1931; abstr., J. A. M. A. **98**:852 (March 5) 1932.

Gangrene of Extremities in Diabetic Patients. P. Escudero and G. Peco, Semana méd. **38**:1899 (Dec. 24) 1931.

Gangrene of Extremities in Nondiabetic Patients: Clinical Study. P. Escudero and G. Schultz Ortiz, Semana méd. **38**:1914 (Dec. 24) 1931.

Gerson-Hermannsdorfer-Sauerbruch Diet in Tuberculosis of Skin: Results. E. Bruusgaard and E. Hval, Norsk mag. f. lægevidensk. **92**:1157 (Nov.) 1931; abstr., J. A. M. A. **98**:860 (March 5) 1932.

Herpetic Virus in Mice: Pathogenicity, Immunity and Susceptibility of Host. H. B. Andervont, J. Infect. Dis. **49**:507 (Dec.) 1931.

Hitherto Undescribed Disease of Skin. A. Whitfield, Brit. J. Dermat. **44**:24 (Jan.) 1932; abstr., J. A. M. A. **98**:1119 (March 26) 1932.

Human and Murine Leprosy in Tropical Australia: Preliminary Notes and Observations. R. W. Cilento and E. A. North, M. J. Australia **2**:767 (Dec. 19) 1931.

Infantile Sudamina or Infantile Miliary Epidemic Exanthem: Its Clinical Aspects and Differentiation from Sudor Anglicus. A. Stroé and H. Stroé, Arch. f. Kinderh. **95**:78 (Dec. 18) 1931.

Remarks on Preceding Article: Likeliness of Identity of Infantile Sudamina and Sudor Anglicus. Rietschel, Arch. f. Kinderh. **95**:89 (Dec. 18) 1931.

Influence of Diet and Anterior Pituitary Growth Hormone on Growth Rate of Adolescent Rats. A. H. Bryan and D. W. Gaiser, Am. J. Physiol. **99**:379 (Jan.) 1932.

Influence of Potassium on Pruritus. J. Sauer, Deutsches Arch. f. klin. Med. **172**:219 (Dec. 21) 1931; abstr., J. A. M. A. **98**:930 (March 12) 1932.

Injection Treatment of Varicose Veins: Three Hundred and Twenty-Five Cases. C. Weeks and R. S. Mueller, Surg., Gynec. & Obst. **54**:98 (Jan.) 1932; abstr., J. A. M. A. **98**:851 (March 5) 1932.

International Comparison of Roentgen-Ray Standards. L. S. Taylor, Radiology **18**:99 (Jan.) 1932.

Investigations on Mode of Action of Potassium. J. Sauer, Deutsches Arch. f. klin. Med. **172**:223 (Dec. 21) 1931; abstr., J. A. M. A. **98**:930 (March 12) 1932.

Irradiation of Carcinoma of Skin and Lips. L. Arzt and H. Fuhs, Wien. klin. Wchnschr. **45**:15 (Jan. 1) 1932; abstr., J. A. M. A. **98**:931 (March 12) 1932.

Leprosy in Child. I. N. Kugelmass, New York State J. Med. **32**:68 (Jan. 15) 1932.

Leprosy in Rosario. F. Carrillo, J. M. M. Fernández and S. Schujman, Semana méd. **38**:1932 (Dec. 24) 1931.

Lichen Urticatus: Differential Diagnosis of Smallpox. H. D. Chalke, Brit. M. J. **1**:7 (Jan. 2) 1932; abstr., J. A. M. A. **98**:1036 (March 19) 1932.

Malariotherapy in Dementia Paralytica Complicated with Diabetes Mellitus. J. M. Obarrio and A. J. Petre, Semana méd. **38**:1989 (Dec. 31) 1931; abstr., J. A. M. A. **98**:1043 (March 19) 1932.

Malignant Lymphogranuloma. G. Jona and G. Dalla Torre, Policlinico (sez. med.) **39**:25 (Jan. 1) 1932; abstr., J. A. M. A. **98**:929 (March 12) 1932.

Mechanism of Asthmatic Attack in Chronic Allergic Asthma. B. Steinberg, J. Allergy **3**:139 (Jan.) 1932; abstr., J. A. M. A. **98**:1031 (March 19) 1932.

Mechanism of Thrombophlebitic Edema. L. M. Zimmermann and G. de Takáts, Arch. Surg. **23**:937 (Dec.) 1931; abstr., J. A. M. A. **98**:765 (Feb. 27) 1932.

Metaphen as Disinfectant of Skin. J. A. Kolmer and M. J. Harkins, Arch. Surg. **23**:1007 (Dec.) 1931.

Modified Silver Stain for Treponema Pallidum. Elena de Galantha, Am. J. Clin. Path. **2**:63 (Jan.) 1932.

Mutual Relation Between Zoster and Varicella. E. Bruusgaard, Brit. J. Dermat. **44**:1 (Jan.) 1932.

Nervous and Mental Component in Cutaneous Disease. J. H. Stokes, Pennsylvania M. J. **35**:229 (Jan.) 1932.

Observations on Formation of Wheals: IV. Influence of Calcium Concentration on Histamine Wheals. W. K. Weaver, H. L. Alexander and F. S. McConnell, J. Clin. Investigation **11**:195 (Jan.) 1932. V. Effects of Variation of Carbon Dioxide Combining Power of Blood on Histamine Wheals. F. S. McConnell, W. K. Weaver and H. L. Alexander, ibid. **11**:205 (Jan.) 1932.

Optic Specificity of Dopa-Oxydase. S. M. Peck, H. Sobotka and J. Kahn, Klin. Wchnschr. **11**:14 (Jan. 3) 1932.

Our Changing Conception of Eczema. B. Shelmire, South. M. J. **25**:67 (Jan.) 1932.

Painful Nodular Growths of Ear. A. A. Fernández and J. L. E. Monserrat, Semana méd. **38**:1693 (Dec. 3) 1931; abstr., J. A. M. A. **98**:930 (March 12) 1932.

Pellagra. W. D. Partlow, J. M. A. Alabama **1**:237 (Dec.) 1931.

Pellagra: Analysis of One Hundred and Two Cases. T. R. Boggs and P. Padget, Bull. Johns Hopkins Hosp. **50**:21 (Jan.) 1932; abstr., J. A. M. A. **98**:1030 (March 19) 1932.

Pellagra: Six Cases. H. B. Fralic, M. Bull. Vet. Admin. **8**:56 (Jan.) 1932.

Pigment Formation in Skin with Especial Consideration of Optic Specificity of Dopa-Oxydase. Bloch and F. Schaaf, Klin. Wchnschr. **11**:10 (Jan. 2) 1932.

Primary Carcinoma of Appendix. O. F. Mazzini, D. Brachetto-Brian and A. Ballestrasse, Semana méd. **38**:2029 (Dec. 31) 1931.

Prophylactic Vaccination Against Tularemia. L. Foshay, Am. J. Clin. Path. **2**:7 (Jan.) 1932; abstr., J. A. M. A. **98**:917 (March 12) 1932.

Protection of Skin Against Light. H. Meyer and H. Kirchhoff, Deutsche med. Wchnschr. **58**:41 (Jan. 8) 1932.

Provoked Extravasation to Determine Resistance of Skin Capillaries. E. Jaso, Arch. españ. de pediat. **15**:720 (Dec.) 1931.

Removal of Cervical Lymph Nodes. J. Heitz, E. Martin and P. Colson, Rev. de chir. **50**:655 (Nov.) 1931; abstr., J. A. M. A. **98**:1039 (March 19) 1932.

Roentgen Therapy in Lymphogranulomatosis. M. I. Karlin, Klin. Med. **9**:898 (Oct.) 1931.

Sclerodermia and Thyroid Tumor. H. Haldin-Davis, Brit. J. Dermat. **44**:29 (Jan.) 1932.

Skin Disturbances in Venous Diseases: Varicose Ulcer. G. Delater, Presse méd. **39**:1808 (Dec. 9) 1931.

Skin Manifestations in Venous Diseases: Edemas. G. Delater, Presse méd. **39**:1690 (Nov. 18) 1931.

Splenomegaly Before and During Chancre. A. Dreyfuss, Ann. de mal. vén. **26**:816 (Nov.) 1931; abstr., J. A. M. A. **98**:854 (March 5) 1932.

Sterilization of Lassar's Paste. A. J. Bandoni and Teresa Satriano, Semana méd. **38**:2040 (Dec. 31) 1931.

Survey of Probable Prognostic Factors in Treatment of General Paralysis. W. A. Caldwell, Brit. M. J. **2**:1129 (Dec. 19) 1931; abstr., J. A. M. A. **98**:771 (Feb. 27) 1932.

Technical Improvement of Obliteration of Varicose Veins. G. Nobl, Med. Klin. **27**:1855 (Dec. 18) 1931.

Thallium Acetate in Treatment of Ringworm of Scalp. J. T. Ingram, Brit. M. J. **1**:8 (Jan. 2) 1932; abstr., J. A. M. A. **98**:1036 (March 19) 1932.

Thallium Poisoning: A Preliminary Report of Eleven Cases at the General Hospital of Fresno County, California. H. M. Ginsburg and C. E. Nixon, J. A. M. A. **98**:1076 (March 26) 1932.

The Use of Vein Ligation in the Treatment of Arteriosclerotic and Diabetic Gangrene. H. E. Pearse, Jr., J. A. M. A. **98**:866 (March 12) 1932.

Treatment of Common Skin Diseases. G. B. Underwood, J. Indiana M. A. **25**:5 (Jan.) 1932.

Treatment of Malaria of General Paralysis of Insane. C. de Asis, J. Philippine Islands M. A. **11**:429 (Nov.) 1931.

Tuberculous Etiology of Erythema Nodosum: Experimental Confirmation. R. Cibils Aguirre, Semana méd. **38**:1673 (Dec. 3) 1931.

Tularemia. Margaret Foulger, Alfred M. Glazer and Lee Foshay, J. A. M. A. **98**:951 (March 19) 1932.

Tularemia (Deer Fly Fever; Rabbit Fever). W. A. Hayward, J. Kansas M. Soc. **32**:407 (Dec.) 1931.

Tularemic Encephalitis: Pathology of Acute Tularemia with Brain Involvement and Coexisting Tuberculosis. F. W. Hartman, Am. J. Path. **8**:57 (Jan.) 1932; abstr., J. A. M. A. **98**:1027 (March 19) 1932.

Two Cases of Erysipeloid. A. Lindaas, Norsk mag. f. lægevidensk. **92**:1217 (Nov.) 1931.

Ultraviolet Radiation Useful for Therapeutic Purposes: Specification of Minimum Intensity, or Radiant Flux. W. W. Coblentz, J. A. M. A. **98**:1082 (March 26) 1932.

Urticaria Solaris. E. Weiss, J. Allergy **3**:192 (Jan.) 1932.

SYPHILOLOGY

Acetarsone in Treatment of Congenital Syphilis. E. Nedelmann, Jahrb. f. Kinderh. **134**:89 (Dec.) 1931; abstr., J. A. M. A. **98**:776 (Feb. 27) 1932.

Antisyphilitic Treatment in Tuberculosis Patients. L. Fisher, Am. Rev. Tuberc. **25**:148 (Jan.) 1932.

Chrysotherapy in Syphilitic Tuberculous Persons. M. Cordier, Lyon méd. **148**:774 (Dec. 27) 1931.

Clinical Aspect of Syphilis of Liver. L. I. Gefter, Sovetskaya med. vostochnoy sibiri, Jan.-Feb., 1931, p. 91.

Incidence of Syphilis in Five Thousand Negro Ex-Service Men. J. B. Garrett and L. B. Smith, M. Bull. Vet. Admin. **8**:38 (Jan.) 1932.

Microscopic Slide Precipitation Test for Syphilis with Spinal Fluid: Comparative Study with Five Hundred Spinal Fluids. J. J. Eller and C. R. Rein, New York State J. Med. **32**:71 (Jan. 15) 1932; abstr., J. A. M. A. **98**:1034 (March 19) 1932.

Mistakes in Diagnosis and Treatment of Syphilis. A. W. Cheever and W. D. Wheeler, New England J. Med. **205**:1249 (Dec. 24) 1931.

Newer Tests of Cerebrospinal Fluid for Differential Diagnosis of Syphilitic Disease of Central Nervous System. A. Marchionini, Klin. Wchnschr. **10**:2393 (Dec. 26) 1931.

Provision for Treatment of the Syphilitic and Gonorrheic. A. Pfeiffer, New York State J. Med. **32**:68 (Jan. 15) 1932.

Problematic Influence of Exfoliative Erythrodermia on Evolution of Syphilis. R. Bernard, Ann. de mal. vén. **26**:807 (Nov.) 1931; abstr., J. A. M. A. **98**:854 (March 5) 1932.

Study of Syphilis in Etiology of Uveitis. P. A. O'Leary, Am. J. Ophth. **15**:24 (Jan.) 1932; abstr., J. A. M. A. **98**:917 (March 12) 1932.

Syphilis of Fetus and New-Born Infant. F. L. Adair, Am. J. Obst. & Gynec. **23**:111 (Jan.) 1932.

Syphilis of Lung: Report of Case with Autopsy Observations. H. C. Denman, Ann. Int. Med. **5**:895 (Jan.) 1932.

Treatment and Course of Neurosyphilis: Case Reports. R. T. O'Neil and F. L. Wright, M. Bull. Vet Admin. **7**:1107 (Dec.) 1931.

Treatment of Yaws and Syphilis. R. U. Gillan, Kenya & East African M. J. **8**:246 (Dec.) 1931.

Yaws and Syphilis: Problems, Clinical Studies and Experimental Evidence Concerning Their Relationship. C. M. Hasselmann, China M. J. **45**:1131 (Dec.) 1931; abstr., J. A. M. A. **98**:926 (March 12) 1932.